Parity and Coronary Heart Disease Risk Factors among Palestinian Women In Two Refugee Camps in the West Bank

Najwa Rizkallah-Khader

Thesis submitted to the University of London
For the degree of Doctor of Philosophy

Nutrition and Public Health Intervention Research Unit
Epidemiology and Population Health
London School of Hygiene and Tropical Medicine
Faculty of Medicine, University of London

October 2008

"I declare that the work presented in this thesis is entirely my own"

[redacted]

Najwa Rizkallah-Khader

ABSTRACT

Background: Evidence from the USA and Europe suggests that women with many births have roughly a 50-80% increase in the risk of developing CHD. The mechanisms underlying this association are unclear, but plausible biological pathways (changes in adiposity, blood glucose and lipid levels associated with pregnancy and continuing after reproduction has ceased) exist. Palestinian women have a greater exposure to high parity than do women in most populations where heart disease and parity have previously been studied, so are expected to be at higher risk.

Objectives: To examine the association of parity with CHD risk factors including obesity, lipids, diabetes and hypertension; MS and reported CHD in a sample of women with a high parity.

Methods: A population based cross sectional survey of 515 Palestinian women aged 40-65 years from two refugee camps communities in the West Bank.

Results: Mean parity was 7.3 (3.69) with a range of 0-21. Prevalence of overall obesity (BMI≥30) was 69.2%, abdominal obesity (WC≥88 cm) was 84.2%, and central obesity (W/H ratio≥0.85) was 51.9%. Prevalence of diabetes was 22.3% and hypertension was 42.7%. After adjustment for covariates (age, own education, husband's education, marital status), regression analyses showed that each extra birth was associated with an increase of 0.30 kg/m^2 in BMI ($p< 0.0001$), 0.58 in waist circumference ($p< 0.001$), and an increase of 0.036 mmol/L in triglycerides ($p= 0.033$). Gravidity, but not parity was associated with fasting blood sugar (FBS); after adjustment for covariates, each extra pregnancy was associated with an increase of 0.14 mmol/L (95% CI: 0.05 to 0.23, $p=0.002$) in FBS. The metabolic syndrome presented in 58.3% of the women. Women with the metabolic syndrome had significantly higher parity and gravidity, ($p= 0.003$ and $p= 0.024$ respectively); each extra birth was associated with a 7% increase in the prevalence of the metabolic syndrome ($p= 0.042$). Parity was not found to be significantly associated with systolic or diastolic blood pressure or with self-reported CHD.

Conclusion: Among these Palestinian women, increased parity is significantly associated with obesity (as measured by BMI and waist circumference), triglycerides and an increased risk of the metabolic syndrome. Any of these, alone or in combination, could result in increased CHD risk for this group of women.

ACKNOWLEDGEMENT

This PhD would not have been possible without the support of many people; to them all I extend my appreciation and acknowledgement.

My greatest thanks go to my supervisor Tom Marshall, who provided scientific guidance, statistical advice and constant assistance. His critical comments enriched my knowledge and experience through the entire process. I am very thankful to him for helping me overcome many of the difficulties I went through during this prolonged PhD process. I also want to thank his wife Katherine and his foster daughter Amanda, who replaced my family while I was away from home; they were always there for me when I needed them.

I am grateful for the friendship of Dr. Oona Campbell, who was my supervisor during the early stages of this study and who supported me and stimulated my thinking in identifying and developing my PhD topic to include both reproductive health and nutrition aspects of women's health.

To Dr. Elaine Meilahn, who acted as a temporary supervisor while Dr. Campbell was teaching at the AUB in Lebanon, I appreciate her scientific guidance and critical comments. I am grateful to her as she has introduced me to the work of Dr. Roberta Ness, Professor Elizabeth Barrett-Connor, Dr. Donna Kritz-Silverstein and others that have inspired my work and thinking and helped me to develop my research proposal. She used to draw my attention to new references whenever she hears or reads about them.

Special appreciation goes to Professor Elizabeth Barrett-Connor and Dr. Donna Kritz-Silverstein from the University of California, San Diego, for reviewing parts of my draft thesis and for providing valuable comments and encouraging complementary words.

Special thanks goes to UNRWA health officials for giving permission for the study to be conducted; to the nurses and doctors at UNRWA clinics at both the Amaari and the Kalandia refugee camps, who facilitated my work and who suffered the extra burden of working hours; to community leaders and women activists at both camps who facilitated my fieldwork; to the fieldwork team, who worked constantly and under very difficult circumstances. Special thanks also go to the women in the camps who participated willingly and enthusiastically in the study and who provided continuous support with a

smile, in spite of their sufferings and mourning. To all of you, I extend my deep appreciation and thankfulness.

Special thanks to my colleagues at the Epidemiology and Population Sciences department for their emotional support and understanding: Amira, Karen, Irma, Sofie, Ebbi, Nadia, James, Anna. To EPH computing support team at London School of Hygiene and Tropical Medicine for their kindness and support, and to Elaine Williamson for her continuous support and kindness.

Back in Palestine, I am grateful to a number of people and organizations who have helped at various stages of the research, whether as team members or in data entry or editorial assistance and in providing articles through their connections with university websites: Alpha for consultancy work, Monica Awad, Samar Yasser, Professor Ziad Abdeen, Radwan Qasrawi, Joan Jubran, Maha Abu-Ghosh, Waheeb Hanani, Sandra Rasheed and Anita Khoury.

Special thanks also go to Dan Rohrmann, Special Representative-UNICEF office in occupied Palestinian territory, for his support and for giving me the opportunity to take leave without pay from UNICEF in order to finish my PhD.

This work would not have been accomplished without the financial support of many different sources. I am thankful to Ford Foundation for their generous support and patience; to the British Council both at UK and Occupied Palestinian Territory for supporting part of my studies in London; to MEAwards, Population Council Research Grant, West Asia and North Africa, in Cairo for financing the field work; and finally for the Palestinian American Research Council (PARC) for making the completion of this study possible. To all those I extend my deep appreciation.

Finally I would like to extend my greatest appreciation to my mother Leila, my aunt Nadia, my sisters Sofia and Norma and my brothers Salim and George and their families for their support and love all the way through this hard work. I also want to thank my mother-in-law, Rasmieh, and sister-in-law, Aida, for their continuous support, love and care. Most of all, I want to thank my beloved husband Sami Khader who has made, along with my children, many sacrifices to help me complete this work. His love, tolerance, understanding, continuous support and encouragement is really rare to find in this world. To my beloved children Faris, Amer and Shadi, I appreciate you bearing with me many missed weekends and summer vacations and many other opportunities of

being all together. I am blessed to have such a wonderful family and great extended family support and love of which I am very proud. Without their constant support, this work would never have come to an end.

Finally to the souls of my father and grandmother, who always wanted me to become as Dr. Rizkallah. Their support has nourished my learning abilities and ambitions to go for the PhD, while their challenging comments and continued inspiration, equipped me with the needed perseverance to become who I am today. To their souls, I dedicate this work.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

List of Maps

LIST OF APPENDICES

GLOSSARY OF TERMS AND ABBREVIATIONS

BMI	Body Mass Index
CHD	Coronary Heart Diseases
CI	Confidence Interval
CP	Contraceptive Pill
CVD	Cardio Vascular Diseases
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
FBS	Fasting Blood Sugar
HDIP	Health, Development, Information and Policy Institute
HDL-C	High Density Lipoprotein Cholesterol
HRT	Hormone Replacement Therapy
IDF	International Diabetes Federation
IMT	Intima-Media Thickness
LDL-C	Low Density Lipoprotein Cholesterol
MI	Myocardial Infarction
MOH	Ministry of Health
MS	Metabolic Syndrome
NGO	Non-Governmental Organization
NGT	Normal Glucose Tolerance
NHEFS	National Health Epidemiological Follow-up Study
NHP	National Health Plan
OC	Oral Contraceptives
OR	Odds Ratios
PCBS	Palestinian Central Bureau of Statistics
PHC	Primary Health Care
PLO	Palestinian Liberation Organization
PMRS	Palestinian Medical Relief Society
PNA	Palestinian National Authority
SBP	Systolic Blood Pressure
SCD	Sudden Cardiac Death
SHIP	Study of Health in Pomerania
SMR	Standardized Mortality Ratio
T-Chol	Total Cholesterol
Tchol/hdl	Total Cholesterol/HDL-C ratio
TFR	Total Fertility Rate
TG	Triglycerides
UN	United Nations
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
UNRWA	United Nations Relief and Works Agency for Palestinian Refugees
W/H ratio	Waist Circumference/Hip Circumference ratio
WC	Waist Circumference
WHO	World Health Organization
WHR	Waist/Hip Ratio

ORGANIZATION OF THESIS

The thesis is divided into fourteen chapters. **Chapter one** provides a brief background, aim, rationale, and research objectives of the study. **Chapter Two** reviews the geopolitical environment and the demographic characteristics particular to Palestine and the Palestinian refugee camps. **Chapter Three** focuses on the development of the Palestinian health care system in the second half of the 20th century under different administrations, the role of non governmental institutions, improvements under the Palestinian Authority since 1994, recent difficulties in health care in Palestine, and the consequences of the unstable political situation and its impact on the health sector. Palestinian women's health and cardiovascular diseases in Palestine are discussed in **Chapter Four.**

Chapter Five presents the review of literature in two parts: the first part highlights the literature review search strategy and then discusses cardiovascular diseases, the major classical risk factors for coronary heart disease and addresses the question, "*why are women special?*"

The second part of the literature review covers the epidemiological association between high gravidity, high parity and early age at first birth and increasing risk of coronary heart disease in women (CHD morbidity and mortality in women). It goes on to discuss some of the likely biological mechanisms between reproduction and coronary heart disease, as well as the methodological difficulties involved in interpreting the results from such studies. Based on the results found in the literature reviewed, a conceptual framework for the thesis was developed with justification, objectives and research hypotheses.

In **Chapter Six,** some of the difficulties of undertaking research in the Palestinian context and particularly in the fieldwork for this study are presented. It summarizes the research methodology and the preparatory work prior to work in the field, describes the targeted refugee camps and the study population, the sampling frame, the data collection methods and instruments used. This is followed by a description of the data collection logistics, the analytical framework and the statistical methods used.

The results of the study begin in **Chapter Seven** by presenting the demographic, socio-economic and health characteristics of the study population and how some characteristics are linked to parity. Chapters Eight to Thirteen explore in more depth

how parity is associated with each variable under analysis using different statistical models: **Chapter Eight** indicates the characteristics associated with different anthropometric measurements and presents further analyses for each anthropometric indicator with parity. **Chapter Nine** presents the characteristics associated with elevated lipid levels and presents further analysis for the various elevated lipid levels with parity.

In **Chapter Ten** Type II diabetes mellitus is investigated by looking at its associated characteristics and then by further analysis of its development with parity and also gravidity. The chapter gives a justification for taking gravidity (number of pregnancies) rather than parity (number of children) when looking at the case of fasting blood sugar and diabetes, and expands the analysis to explore other characteristics and mediators. **Chapter Eleven** presents the characteristics associated with elevated SBP, DBP and hypertension, then discusses further analysis of each of the blood pressure components (SBP and DBP) with parity. **Chapter Twelve** describes characteristics associated with women's reports of CHD and then presents further analysis of parity with reported CHD. **Chapter Thirteen** gives the characteristics associated with the metabolic syndrome and continues to present further analysis of the metabolic syndrome and parity, considering other characteristics and mediators.

The **concluding chapter** presents a general discussion of the thesis, including the relevance of the work carried out, beginning with a summary of the main findings followed by a description of the uniqueness of the study. Methodological considerations are addressed including the strengths and limitations of the approaches used. This is followed by a discussion of the common themes in the association between parity and each of the CHD risk factors, as well as reported CHD and the metabolic syndrome. Finally the implications for public health are presented and discussed.

FUTURE PUBLICATIONS

1. Number of children and risk of metabolic syndrome among Palestinian women living in refugee camps.
2. Does educational attainment play a role in the development of the MS among Palestinian women?
3. Parity, Gravidity and the development of type II diabetes in Palestinian refugee women.
4. Is it failed pregnancies rather than parity that predict the development of type II diabetes mellitus among Palestinian women?
5. Does parity increases the risk of CHD in women?
6. Does women's education decrease the risk of CHD?
7. Does women's education reduce parity and gravidity?
8. Which anthropometric indices predict the MS in women?
9. Which of the anthropometric indices BMI, WHR and WC could predict CHD risk in women?
10. Parity and coronary heart disease risk factors among Palestinian women in two Refugee camps of the West Bank.
11. Gravidity, rather than parity and incomplete pregnancies predict diabetes mellitus in women.

Chapter 1
INTRODUCTION

1.1 Background to the Study

Coronary heart disease (CHD) is the most common cause of mortality in many developed and developing countries [1]. Research and major intervention trials in the United States and Europe have focused primarily on men, since they, on average, develop CHD earlier than women. This has been the case also because women are considered relatively protected from CHD until menopause as sex hormones appear to modify the impact of risk factors on the disease [2].

New research has increased the profile of CHD as an important issue for women. More women die of circulatory diseases than from all forms of cancer, including breast cancer, ovarian cancer and cervical cancer [3] [1]. Epidemiological studies have indicated that women in the West share major CHD risk factors with men. These include elevated serum cholesterol levels, hypertension, and cigarette smoking. Yet women may have additional risks unique to their gender including exposure to endogenous and exogenous hormones through menstruation, pregnancy, breastfeeding, menopause, oral contraceptives and hormone replacement therapy [4] [5].

Reproductive factors have been extensively studied in the context of diseases that occur exclusively in women. Large numbers of studies have examined the aetiological roles of reproduction in breast and ovarian cancers. Yet there has been relatively little examination of childbearing and other reproductive factors as risk factors for CHD. Evidence from the USA and Europe suggests that women with many births have roughly a 50-80% increase in the risk of developing CHD. The mechanisms underlying this association are unclear, but plausible biological pathways exist (changes in adiposity, blood glucose and lipid levels associated with pregnancy and continuing after reproduction has ceased) [6] [7] [8]. Confounding factors such as socio-economic status which could be related to both the exposure (gravidity/parity) and the outcome of Interest (CHD morbidity and mortality) may account for at least some of the reported association as well.

What little evidence exists, suggests that like many other developing countries, Palestine has at least partially broken the cycle of poor sanitation, malnutrition, high infant mortality rate and modest life expectancy, to create a "health transition" characterized

by a growing adult and elderly population and an increasing incidence of chronic disease. Routine statistics as well as small scale studies (cited below) show high prevalence rates of CHD, diabetes, hypertension, and obesity for all areas of Palestine including the West Bank and Gaza Strip.

According to the Palestinian National Authority (PNA), Ministry of Health Annual Report [9], heart diseases are the first leading cause of death among the general population, males and females, at 55.3% and 44.7% respectively in the West Bank and Gaza Strip. Ischemic heart disease is the leading cause of cardiovascular mortality (36.1%) with a rate of 36.4 per 100,000 population. Mortality among males is higher than females (57.7% vs. 42.3%) with a rate per 100,000 in males 41.5 and 31.2 in females. The data here though is not segregated by age group [9].

Risk factors for CHD and CVD appear to be common among Palestinians. The prevalence rate of Diabetes Mellitus in Palestine was 9% [10]. According to the United Nations Relief and Works Agency (UNRWA) department of health annual report [11], the prevalence of diabetes mellitus among refugee camps population of the West Bank was 6.03%. The prevalence of hypertension was reported to be 8.22% among the adult refugee population above 40 years of age in the West Bank. The report also stated that 68% of individuals with hypertension or diabetes were obese (BMI >30). A population based cross sectional survey showed that the prevalence of obesity (BMI $\geq$ 30) was 36.8% and 18.1% in rural Palestinian women and men respectively [12]. Recent statistics from UNRWA indicates prevalence rates of diabetes mellitus and hypertension among refugees attending UNRWA clinics 40 years and above at 10.5% and 14.3% respectively [13].

Very little systematic information is available in the area of adult women's health in Palestine. A cross-sectional household survey of the socio-economic and health profile of Palestinian Arab Inhabitants of the old city of Jerusalem showed that 15% of the sampled 1334 individuals of all ages reported suffering from diabetes, hypertension, orthopaedic problems, CHD and arthritis [14]. Women in the sample aged 40 and above reported higher rates of diabetes, hypertension, and a combination of one or more of chronic diseases, such as diabetes and hypertension, hypertension and CHD compared to men of the same age.

Despite evidence for a big burden of chronic disease which appears to affect women as well as men, the national and international development programmes have overlooked

long term health needs of women. Women's health for many years has been equated with only pregnancy and childbirth in Palestine. This functional view of the role and cause of existence of women has led to the omission of a whole range of health services needed by women at different stages in their lives.

The focus on childbearing may in part stem from the high annual birth rate. The Palestinian Central Bureau of Statistics (PCBS) reported a crude birth rate of 45.9 per 1000 population for the West Bank and 53.9 for the Gaza Strip during 1993 [15], and a total fertility rate of 6.84 births per woman [16]. In comparison, the total fertility rate in the UK was 1.8 at the time this study was conceived in 1997. In 2006, the crude birth rate in Palestine was 36.7 (41.7 in Gaza Strip and 33.7 in West Bank) per 1000 population [17]. The fertility rate in 2006 was also high at 4.6 births per woman (5.4 in the Gaza Strip and 4.2 in the West Bank) [18] [19].

The available data on the health of Palestinian women suggests the largest gaps in research and services exist in the area of chronic diseases. Nevertheless, Palestinian women's childbearing patterns are different from those typically seen in North America and Europe and may play a different role in contributing to chronic diseases.

1.2 Aim of the Study

This study aims at exploring the relationship between parity and coronary heart disease risk factors among Palestinian women in the refugee camps. To our knowledge, it is the first of its kind in the Middle East region in general and Palestine in particular to look at the long term effect of reproduction on women's health. Numbers in the age group at risk are increasing, thus requiring additional efforts aimed at health promotion and primary prevention of coronary heart disease among Palestinian women. It also provides an extra rationale for reducing high fertility.

1.3 Rationale for the Study

Most of the epidemiological studies which have looked at the relation between parity and risk factors for CHD have been conducted either in Europe or the USA. However in those settings few women give birth to 5 or more children, which may make it difficult to detect any association. In addition, it is unclear whether one can extrapolate findings from these countries to the Arab world where women have different life styles, diets and different exposure to reproductive and environmental factors.

The present study examines the association between parity and known risk factors for CHD among Palestinian women, against a background of a total fertility rate of 6.84 births per woman at the time the study was conceived [16]. The most recent report states that the rate is now 4.6; 5.4 in Gaza Strip and 4.2 in West Bank [19]. Palestinian women have had and still have a greater exposure to high parity; gravidity and early age at first live birth than most populations where heart disease and parity have been studied, which makes it an ideal population for extending studying of this issue. In addition, as has been shown above, chronic diseases, in particular CHD, are the leading cause of mortality and morbidity among Palestinian women as well as its associated risk factors obesity, hypertension and diabetes. Although Palestinian society is characterized as being youthful, it is becoming older and both the proportion and the absolute number of middle aged and obese women is increasing [20]. Fertility is falling, so this trend to a larger proportion will continue. There will be more women in the high-risk age groups for chronic diseases including CHD. Additionally, Palestinian women may be at excess risk of CHD and diabetes relative to women elsewhere because of a childbearing pattern of early age at first pregnancy as well as high parity. Results from this study can provide population-based estimates of the prevalence of CHD risk factors in Palestinian women. It is the first study in the Middle-East in general and Palestine in particular, to look at the long term effect of reproduction on women's health. Understanding the unique aspects of risk for Palestinian women will increase the awareness of women and medical caregivers and will pave the way for primary prevention efforts.

Further to the above points, this research falls within three priorities: unstable areas, reproductive health, and chronic diseases. As the Palestinian Authorities have taken over responsibility of health, they face a severe lack of basic health data. Such a situation makes them particularly susceptible to international donor priority setting. For example, the international reproductive health agenda in the Middle East promotes work on STD, HIV, female circumcision and family planning. The limited data available in Palestine suggest that only the latter (family planning) is a major problem. By contrast, anecdotal data and statistics from the Palestinian Ministry of Health suggest chronic diseases are common. By describing the prevalence of CHD risk factors, showing their impact on women's lives, and clarifying the relationship between reproduction and CHD risk factors, basic data to support the Palestinian Ministry of Health will be provided, which is useful in evidence-based decision making and allocation of health care resources, and can contribute to health promotion and primary prevention of CHD

among Palestinian women, both to increase public awareness to the burden placed by chronic diseases, and to provide one more health rationale for reducing high fertility.

Given the limited availability of resources, this research can also help prioritise the most effective interventions for prevention and treatment of these women.

1.4 Research Objectives

- To measure blood pressure, serum lipids, body height and weight, body fat distribution and diabetes mellitus among Palestinian women. From these measurements to derive standard risk scores for these women.

- To estimate the prevalence of obesity, diabetes mellitus, hyperlipidemia and blood pressure among these women.

- To assess the relationship between parity and the above mentioned risk factors for CHD.

- To identify women at greatest overall risk of developing coronary heart disease (CHD) using the derived standard risk scores.

- To examine if parity contributes to the development of the metabolic syndrome in these women.

- To examine if parity contributes to the development of CHD events in the form of women's reports of present or past CHD.

- To estimate CHD risk for the next 10 years by using the Framingham risk score.

Chapter 2
PALESTINE: GEOPOLITICAL ENVIRONMENT AND DEMOGRAPHIC CHARACTERISTICS

The structure and capacity of the Palestinian health system have been marked sharply by the country's political history. The recent development and planning for the health sector have been always effectuated under uncertain and very difficult conditions, sometimes under emergency situations lasting for long periods. To understand the root causes of the current obstacles faced, a description is necessary first of the geopolitical context and historical evolution of the Palestinian health system.

2.1 Geopolitical Environment

The Palestinian territories are compromised of two separate geographic areas with different demographic, economic and even legal status: the West Bank and the Gaza Strip separated by the State of Israel (See Map 2-1).

Map 2-1: The West Bank & Gaza Strip

The population density in the Gaza Strip is ten times more than that in the West Bank. The population of Gaza Strip lives in 28 towns, villages and refugee camps, with one of the highest population density in the world of 3,505 inhabitants per square kilometre, with 66.1% refugees. In the West Bank, there are about 600 towns, villages and refugee camps with 380 inhabitants per square kilometres with about 28.9% of the population consisting of refugees [21].

Health inequalities are obvious between the West Bank and the Gaza Strip. The current total fertility rate is 4.6: 5.4 in the Gaza Strip and 4.2 in the West Bank [19]. The infant mortality rates are 28.8 and 22.9 per 1000 live births in the Gaza Strip and the West Bank respectively [19].

Poverty rates in Gaza remained higher than those in the West Bank. The estimates by the World Bank for September 2006 demonstrate that poverty rates have been increasing significantly from 43% in 2005 to 67% in 2006 [22] and the Bank states further that Palestinians living in the Gaza Strip are far more likely to be poor (23%) than individuals living in the West Bank [23].

In addition, urbanization has been increasing as more people move to urban centres seeking their livelihood or to avoid the need for travelling from and to workplaces with considerable access problems.

These geographical disparities are exasperated by the political development of the past several years, which have affected health planning in Palestine, in general, and planning for women's health in particular, especially when two separate *de facto* health systems have been created (see below).

2.2 Demographic Characteristics of Palestine

In 2008, the total Palestinian population reached 3,761,646 [24]. According to the population pyramid, Palestinian society is one of the youngest in the world, with 45.5% at an age less than 15 years old [24]. The pattern of the age distribution is similar to the patterns of countries of high fertility rate. Life expectancy during the year 2006 was 72.6 years and the median age remained the same during the period between 1995 and 2006 at 16.7 years. Females constitute 49.3% [19].

It is worth noting that the total fertility rate in Palestine is still among the highest, at 4.6. Because Palestine is among those societies where women marry at relatively early ages fertility rates tend to be high.

2.3 Demographic Characteristics of Palestinian Refugee Camps

According to UNRWA, "Palestine refugees are persons whose normal place of residence was Palestine between June 1946 and May 1948, who lost both their homes and means of livelihood as a result of the 1948 Arab-Israeli conflict." UNRWA provides services "to all those living in its area of operations who meet this definition, who are registered with the Agency and who need assistance. UNRWA's definition of a refugee also covers the descendants of persons who became refugees in 1948." The number of registered Palestine refugees in Jordan, Lebanon, Syria, Gaza Strip and the West Bank has grown from 914,000 in 1950 to more than four million in 2002, and continues to rise with natural population growth.[25]. Population growth continues; in 2005, this number reached 4,349,946 representing an overall increase of 2.7% since 2004. In 2007, the number of the refugee population reached 4,562,820 representing an increase of 2.5% compared to 2006 [26]. More than 45% of the population are registered refugees. One third of these registered refugees live in 58 official camps, in Jordan, Lebanon, Syria, and the Gaza Strip and the West Bank. The remaining population lives in unofficial camps, towns and villages of various host countries [27].

The demographic profile of Palestinian refugees is that of a young population with children below 18 years of age constituting 39.3% of the total population, and as high as 48% in the Gaza Strip . Women of reproductive age (15-49 years) constitute 24.7% of the total refugee population.

The specificities of the refugee population in the West Bank and the Gaza Strip are unique and vary from other host countries (Lebanon, Syria and Jordan). According to an UNRWA study conducted in 2005, the average family size for the refugee populations in all these countries dropped from 5.85 in 1995 to 5.26 in 2005. But the largest family sizes were in the West Bank at 5.77 and in Gaza at 5.75. Total fertility rates showed a significant decline as well over the last two decades reaching 3.2 amongst all refugee population in all countries, with the highest rate of 4.6 in the Gaza Strip [28].

The refugee population in all countries has witnessed improvement in fertility rates, a decline in infant and child mortality rates and an increased life expectancy, but is facing increased poverty and unemployment rates, which will most likely result in higher dependency ratios, reaching 77.1% in the West Bank and 100% in the Gaza Strip [27].

Chapter 3
PALESTINIAN HEALTH CARE SYSTEM

The current Palestinian health system with its main players has been formed by the long years of colonization and military occupation.

During the British Mandate (1920-1948), some government hospitals and health clinics were provided for the Palestinians but the British colonial policy aimed at limiting the development of health services [29]. And this system collapsed in 1948 at the aftermath of the Arab-Israeli War resulting in the emergence of two separate health systems, as Jordan ruled the West Bank while Egypt administered the Gaza Strip [30]. Moreover at that time, three quarters of a million Palestinians became refugees [29] which led to the creation of the UNRWA in 1949 by the United Nations General Assembly. This started its' operations in 1950 to "carry out direct relief and works programmes for Palestine refugees" [31]. UNRWA therefore began providing more modern health services (mainly curative and rudimentary) to refugees.

Following the 1967 occupation of the West Bank and the Gaza Strip, the Israeli occupation represented by the Israeli Civil administration managed the governmental health care system. Another two important periods were the establishment of the Palestinian Authority in 1994 and the start of the second Popular Uprising (Intifada) in September 2000.

3.1 Israel's Administration of the Health Sector (1967-1994)

Before the 1967 occupation of the West Bank and Gaza by Israel, three different health systems were operating. The government of Jordan supervised the public health system in the West Bank, Egypt managed the system in the Gaza Strip and UNRWA provided health services for refugees. In addition, the private sector, including at that time charitable organizations administered main hospitals, diagnostic centres and primary care centres.

Following the occupation, the governmental health care system was taken over by the Israeli Civil Administration and the system remained totally dependent on the Israeli health system due to Israel's policy of severe budget restrictions, referral to Israeli hospitals for tertiary care and restrictions on licenses for new health care projects. Hospitals and health facilities were closed and institutions were not developed to meet

the changing local needs of the Palestinian population. The health system was characterized also by the disempowerment of Palestinians in decision-making and top-level management [32].

The overall health status was inadequate. During the late 1970's and early 1980's, infant mortality was high, estimated at 50-100 deaths per 1000 live births. Morbidity levels were also high and the rate of malnutrition was 50% among children in some communities [33].

This period was mainly characterized by the complete control and dominance of the Israeli occupation and its policy towards the health sector of not allowing any future development to take place. This led to health civil society movements appearing as a reaction to the severe restriction by the Israeli occupation.

3.2 Independent Palestinian Initiatives

In response to the acute needs of the population, grassroots popular health committees, affiliated with Palestinian political movements, emerged in the late 1970s and took root in the early 1980s. They aimed at building independent Palestinian institutions to respond to the health needs reaching out to underprivileged populations with volunteer health providers and building an independent Palestinian health infrastructure [34]. These initiatives concentrated mainly on preventive and health education activities while advocating for people's participation in addressing health problems. As a result, new concepts and methods in health care provision were introduced based on enhancing mainly primary health care.

Currently, these non-governmental initiatives compromise one of the major health care providers in Palestine and participate actively in national policy making and model developments in cooperation with the Ministry of Health.

3.3 Improving the Palestinian Health Sector under the PA (1994-2000)

Following the signing of the Oslo agreement in September 1993 between Israel and the Palestine Liberation Organization (PLO), the governmental health system of the Gaza Strip previously managed by the Israeli Civil Administration was managed by the Palestinian National Authority (PNA) in 1994 [35]. This period marked the first health planning at a national level and development efforts focused on cooperation between

various health care providers (government, UNRWA, NGO, and private), upgrading and expanding heath infrastructure, institution building within the Ministry of Health, quality control and human resource development in the West Bank and Gaza. Moreover, a national health information system was developed. A government health insurance scheme was initiated and training was carried out in certain areas such as women's health. Different policies, guidelines and protocols in various national health issues, such as maternal and child health, were also developed. Participatory planning with the four service providers was undertaken intensively.

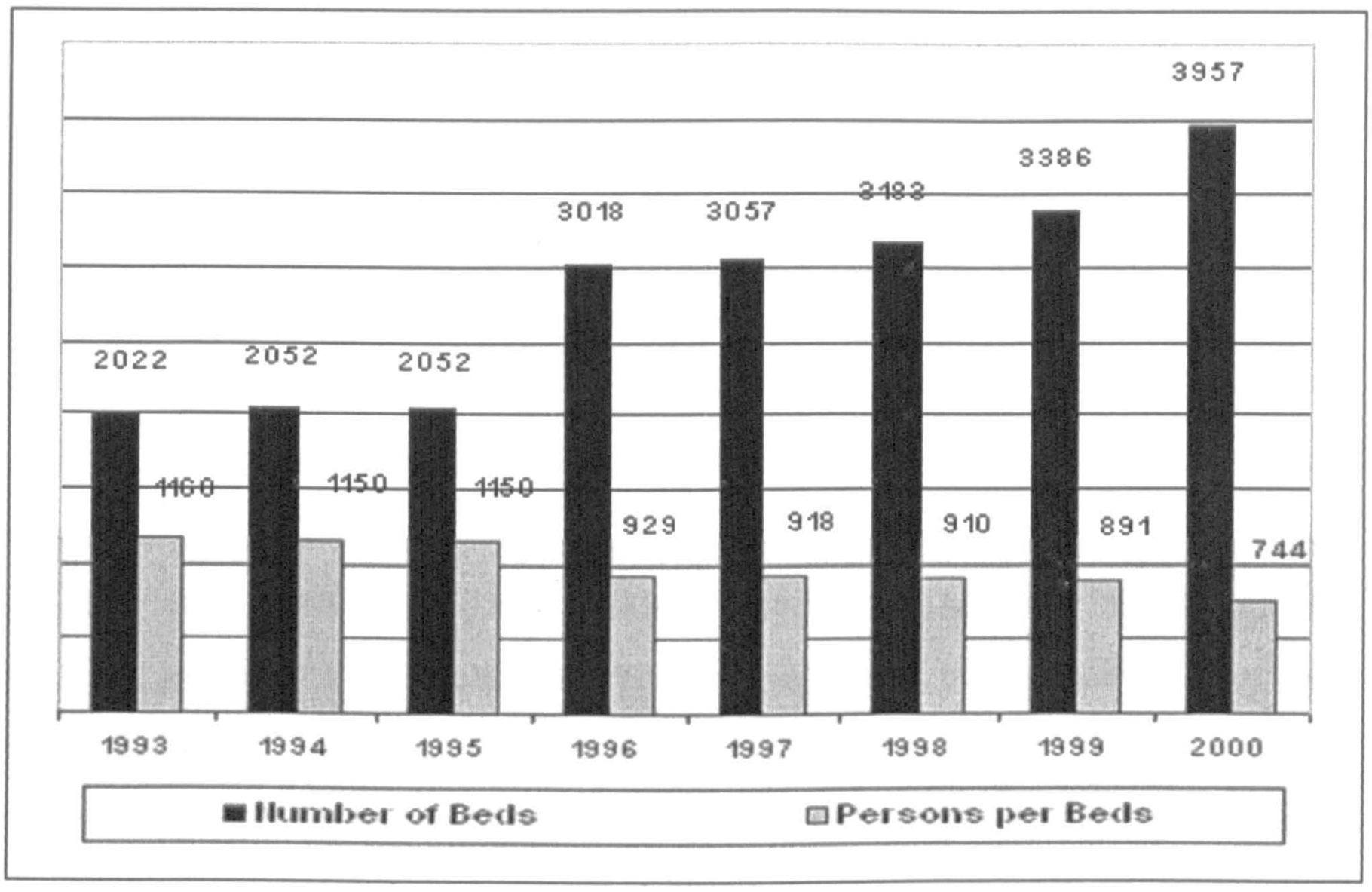
The first health planning processes at a national level emerged and led to the formulation of a first National Health Plan (NHP) produced in April 1994. However, it was only an initial plan with little connection with reality. The political, social and professional context contributed to the limited ability of the MOH to implement the original plan. In May 1999 a new version of the NHP was published [36].

It is important to highlight three significant indicators as examples underlining the accomplishments prevailing during this period: the increase in the number of hospitals and primary health care centres, the extended coverage of health insurance as well as the cooperation initiatives between NGOs and the government. These had a direct impact on the status of Palestinian women and accessibility to health services for this group.

3.3.1 Increase in the Number of Primary Health Care Clinics and Hospitals

There have been considerable efforts in constructing new hospitals. Currently, there are 76 governmental, non-governmental, UNRWA and private hospitals in Palestine. The population/hospital ratio is 45,586 population per hospital and the total number of beds is 4203 (excluding psychiatric hospitals). As indicated in Figure 3-1 below, the number of beds has increased sharply since 1995 [37].

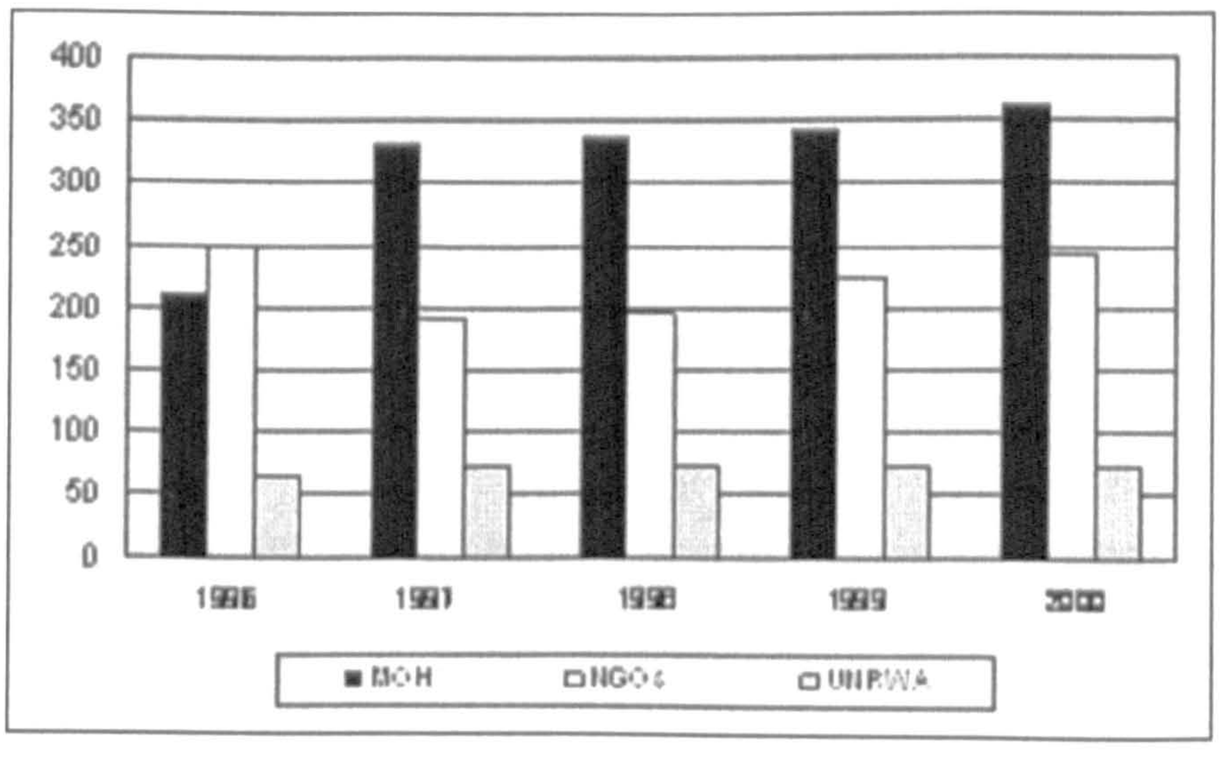
Figure 3-1: Number of Beds and Population per bed in Palestine, 1993-2001



The number of governmental primary health care clinics also increased from 207 to 365 between 1994 and 1998 in the West Bank and Gaza. Due to the decrease in NGO primary health care clinics during this period, the increase was greater in Gaza and the overall number of clinics in the West Bank did not change as much.

Several NGO/MOH clinics functioned jointly and this period saw increased efforts of coordination between the four service providers [38]. Figure 3-2 shows numbers of PHC centres by provider in Palestine since 1996 until 2000. It is clear from this graph that the number of NGO clinics, decreased considerably between 1996 and 1997, whereas governmental clinics increased throughout the period [39].

Figure 3-2: Number of PHC Centres by Provider, 1996-2000



Many new services were introduced into governmental centres among which were family planning services, which were gradually integrated into about one hundred of the newly established governmental clinics.

3.3.2 Expanded Coverage of Governmental Health Insurance

Between 1994 and 1998, the Ministry set up as a priority expanding government health insurance and succeeded in increasing the number of adherents from 25% of households to 48% to include mandatory participation of governmental employees.

However, in the second half of 1997, the Ministry of Health faced a serious financial crisis because the Ministry of Finance failed to allocate the expected budget to the Ministry of Health. This led to deterioration of government services including a lack of essential drugs and supplies and this situation affected public participation in the governmental health insurance programme, which then decreased considerably [40]. The health insurance system lost further one of its major contributors at the beginning of the second popular uprising in September 2000: workers with jobs in Israel who lost their work due to Israeli restrictions to enter Israel and the need for special permits. Voluntary enrolments also decreased and there was a massive increase in social hardship cases enrolled automatically in the insurance system, which led to a decrease in the general revenues of health insurance.

3.3.3 Cooperation and Coordination among Health Care Providers

Since 1994, relations between service providers have been mainly characterized by cooperation and coordination among health care providers, leading to partnerships made between the Palestinian MOH and a number of NGO service providers. These partnerships aimed at avoiding duplication of services and at achieving complementarity within a comprehensive national health plan. Attention was given to national health planning, the optimal use of the available resources, influencing health policies as well as the standardization of operational systems, protocols and standards. National systems have been achieved in school health, women health and other areas.

3.4 The Turning Point: From September 2000 up to date

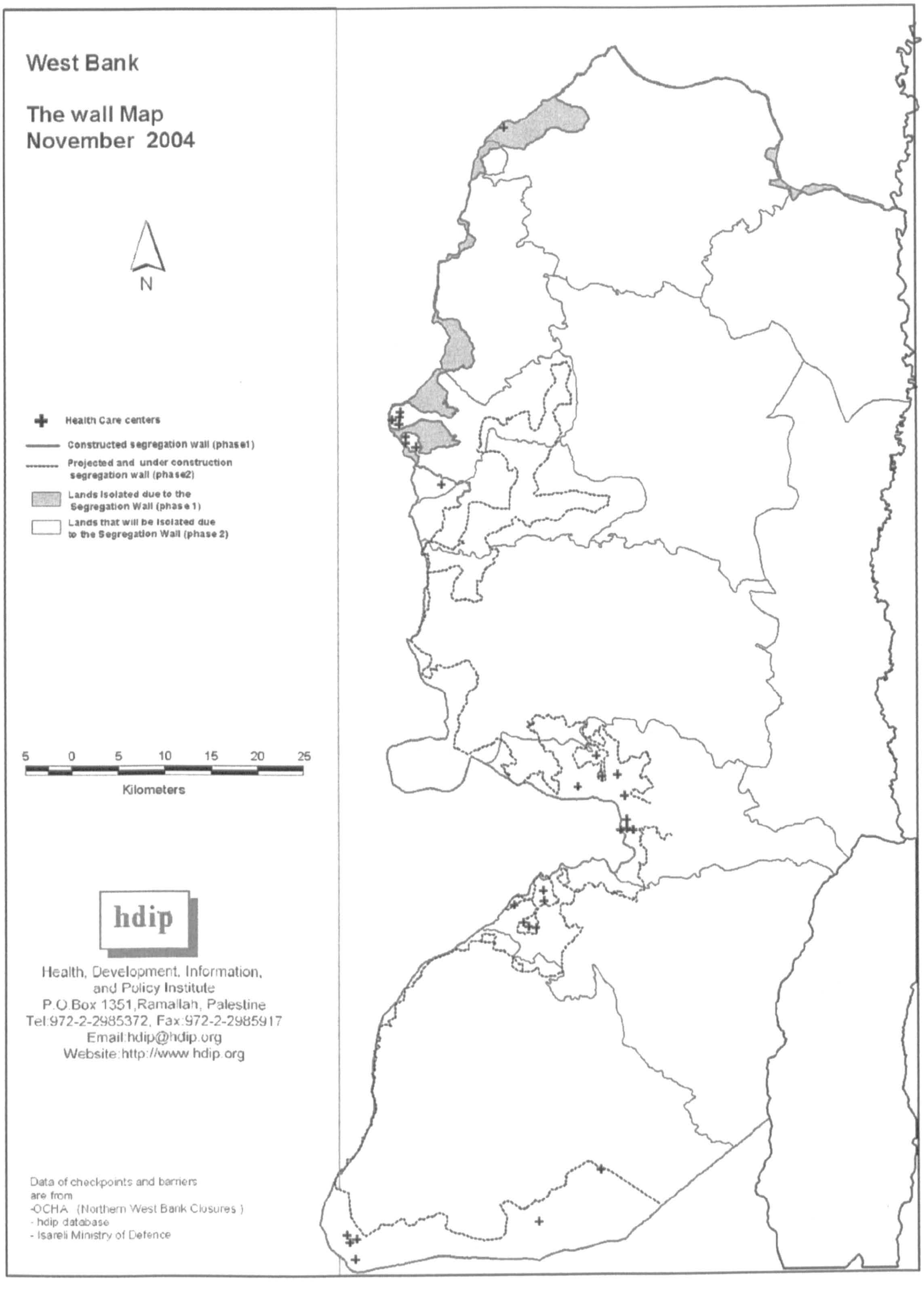
From September 2000 until 2004, a health system crisis emerged with around 4,000 Palestinians dead and around 45,000 injured, also with infrastructure, including hospitals and clinics, being destroyed and shelled by the Israeli army. This situation led

to very severe undermining of already fragile public institutions and services and influenced greatly the health of Palestinians as well as the nature of the Palestinian health care system.

On top of this, in July 2002 the Israeli government began the construction of its West Bank Separation Wall (See Map 3-1). The wall redefines the occupied territories creating new humanitarian problems and needs since mostly it does not follow the 1967 borders, "the Green Line". And according to the latest maps published by Israel, the total length of the Wall, when completed, is estimated to be 622 kilometres [41]. The wall penetrates deep into Palestinian territory resulting in the creation of an isolated zone between the Green Line and the wall. This zone has been designated by Israel a 'closed zone' implementing a permit system for those living or owning land in the area. This zone has also effected the Israeli confiscation and annexation of large tracts of lands, impacting severely on Palestinian agriculture, trade and economy. The construction itself has also led to large-scale destruction of Palestinian property. Olive and citrus trees have been uprooted and agricultural land reduced to wasteland. The Wall isolates thousands of Palestinians into enclosed enclaves cut off from the West Bank presenting problems of inaccessibility to medical, health, social and educational services.

The impact of the Wall affects the health status of Palestinian communities and damages the entire structure of the Palestinian health care system [42]. According to HDIP's estimates, the Wall will affect 750,000 Palestinian people (including Palestinians in East Jerusalem) in nearly 40% of Palestinian communities and has had a serious effect on Palestinian healthcare. The healthcare system in the Palestinian Territories has been developed according to models proposed by the World Health Organization, whereby clinics providing differing levels of healthcare are located in various villages, towns and cities and are supported by a carefully planned referral system. With the Wall's construction, this referral system has been almost completely destroyed because, whereas in the past patients would have been referred to alternative clinics to seek specialized health care, now they are unable to reach these clinics due to the movement restrictions created by the Wall.

Map 3-1: West Bank, the Wall Map, November 2004



3.5 Consequences of the Unstable Political Situation and its Impact on the Health Sector

3.5.1 The Double Nature of Health Problems in Palestine

Palestine is located midway between addressing illnesses characteristic to poor third world countries (infectious diseases, malnutrition, etc) and the increasing rates of modern diseases (cardiovascular diseases, diabetes, hypertension and cancer). But also malnutrition among children has increased. A survey conducted by Johns Hopkins University and Al-Quds University for CARE International in 2002 found global acute malnutrition (GAM) protein-calorie malnutrition of 9.3% of children across the West Bank and Gaza. The study also revealed that 17.5% of children aged 6-59 months suffered from chronic malnutrition. 53% of women of reproductive age and 44% of children were found to be anaemic [43]. Also according to MOH statistics, 9.6% of total births were low birth weight (under 2500 gm), there was 9% prevalence of stunting in children <5 years, 2.5% prevalence of wasting; 6.2% of the population didn't have access to safe drinking water and 54.2% of population of Palestine was not connected to sewer networks. The 2006 Palestinian Family Health Survey reports that one in 10 children less than five years of age is chronically undernourished (stunted), meaning that about 50,000 children will not reach the optimal standards for growth and development. The heaviest burden falls on children between the ages of 1 and 2 (almost 16%), a critical moment in shaping a child's future development [19]. Moreover, as half the Palestinian population has no medical insurance, many Palestinians are now unable to afford medical care [44].

On the other hand, according to PMRS's estimates, 18% of the population has abnormal sugar metabolism, 12% of them suffer from diabetes, 27% hypertension, 27% Dyslipidemia and 75% are overweight [45]. In 2005, the leading cause of death in Palestine was heart diseases, with a proportion of 54.5% [46].

3.5.2 Direct Impact on People's Life

The majority of the population has been living under the severe conditions of unemployment for prolonged times, which has forced many of them to rely totally on assistance to ensure livelihood. Often for coping with such conditions people are forced to resort to borrowing, selling their properties, spending their savings, or decreasing

their spending and consumption of foods and clothing. Seeking health services has become at the top of the list of population needs.

3.5.3 Medical Care: Access Denied

Road blockades have directly prevented patients in need from receiving emergency medical care. More than 1798 incidents of denial of access to Palestinian ambulances have been reported [47]. According to the Palestinian Ministry of Health, between September 2000 and 2004, 129 patients died at Israeli checkpoints and at least 61 women gave birth at Israeli checkpoints. Of these, 5 mothers died while giving birth at Israeli checkpoints and 39 newborns died or were delivered stillborn. Mobile clinics have been regularly obstructed by closures of access roads; with medical staff forced to carry equipment over checkpoints.

In addition, medical personnel often face serious difficulties in reaching workplaces: non-attendance at rural clinics due to closure has been reported at 35-40% in some cases [48]. In 2003, this continued to be the primary reason for health service suspension [49]. Furthermore, promotional and preventive activities such as antenatal care, child monitoring for development as well as vaccination programmes were the most affected. Although several reports indicate that there has been only a slight drop in vaccination coverage, the efficacy of vaccination has been affected from 2000 until 2002 [50]. The increase in measles cases in Gaza, for example, is indicative to the problem linked to efficacy of vaccination programmes during a crisis.

3.5.4 Attacks on Medical Services

Attacks by the Israeli army have been reported on medical personnel, establishments and health related vehicles. Between the 29th September 2000 and May 2006, the Israeli occupying forces carried out the following attacks on Palestinian medical services [51]:

- 846 attacks on ambulances.
- 139 ambulances damaged 28 beyond repair.
- 206 personnel injured.
- 12 medical personnel killed.

3.5.5 Blockade of Materials

The Israeli blockade on goods entering the Occupied Palestinian Territories has had further serious ramifications for Palestinian health services [51]. Health providers have faced great difficulties in the distribution of medical supplies to Palestinian towns and villages. In November 2003, Medicins du Monde reported that UNFPA delivery kits had been held up at Tel Aviv customs since April, and were unable to reach the West Bank. The branch of the Palestinian Ministry of Health in Nablus has been waiting for delivery kits from February until September 2003, during which time they have been delayed [52].

Medical aid has been consistently detained by Israeli border control coming from both Jordan and Egypt. Israeli restrictions have closed the pharmaceutical market to international competition therefore the prices paid by the Palestinian Ministry of Health are notably expensive. The delay of drug deliveries from suppliers and the lack of contact between MOH in Gaza and the MOH in the West Bank, due to movement restrictions have a direct impact on drug procurement. Towards the end of 2002 MOH reported that its facilities were operating at about 30% of their capacity only.

3.6 Funding for the Palestinian Health Sector: Increase of Emergency Aid

Of the total international aid to Palestine, 8% was allocated to the health sector, nearly half of this support coming from Japan (33%) and Spain (15%) [53]. Between 1994 and 2003, US$ 6.7 billion were committed to the West Bank and Gaza Strip by the international community at an average of US$ 670 million per year [54]. But although since the beginning of the Intifada, there has been an unprecedented international commitment by donors providing about US$ 315 per person per year [55], the ability to sustain external support at this level is rather weak. Increasing the size of external donor assistance to reach 2 billions USD during 2003 and 2004 would help decrease poverty only by about 7% [56].

Although several countries have stopped funding the health sector, particularly after 1999, there was a sudden interest of Arab and other foreign countries in donating humanitarian and medical aid supplies from 2000. This included ambulances, medical equipment, blood units, medicines and tetanus vaccinations. Relying on information provided by the Italian Cooperation [57], it was noticed that all health projects throughout the years 2000-2002 were implemented mainly in four areas: the provision

of medical equipment and medical supplies to health facilities, health infrastructure assistance and counselling and psycho-social in projects mainly from Saudi Arabia, Oman, Qatar, Bahrain, United Arab Emirates, Egypt, Algeria, France, Spain and Turkey. Medical teams from Jordan, Saudi Arabia, United Arab Emirates, Egypt, Kuwait, Morocco, Qatar and France arrived in the West Bank and Gaza Strip with equipment to operate in Palestinian hospitals and help treat injuries.

The danger in this context is the continuous pumping of emergency aid consisting of the provision of medical supplies, equipments upgrading infrastructure to cope with an "emergency situation" that has continued for more than six years without attempting to shift towards a more long-term approach of developing the health sector. Specifically during the period October 2000 to midyear 2001, the health sector received US$ 19 million as a humanitarian assistance and US$ 34 million as development assistance [58].

Chapter 4
WOMEN'S HEALTH AND CARDIOVASCULAR DISEASES IN PALESTINE

4.1 Palestinian Women's Health

Since September 2000 and as a direct result of the Israeli-imposed restrictions on the freedom of movement of Palestinians, there has been a continuous decline in women's access to health care. Amongst other things, this has had severe repercussions on women's reproductive health. From September 2000 until October 2004, 61 Palestinian women gave birth at checkpoints, out of which 36 were stillbirths, due to delays or prohibition on travel to medical facilities [59]. Equally, between 2000 and 2003, home deliveries increased from 5.2 percent to over 30 percent [59]. There has been an almost a fivefold increase in the number of pregnant women receiving no pre-natal care due to movement restrictions, and up to 31 percent of pregnant women are anaemic [59].

There has been an increase in births that take place in unsafe conditions or unsupervised by a skilled health worker, all of which has lead to drastic increases in the dangers posed to women during pregnancy and whilst giving birth, and has directly contributed to the infliction of enormous psychological strain on women [60].

The quality of healthcare services has also deteriorated. Overcrowding and overwork in hospitals, particularly government-run hospitals, affect the quality of care given to pregnant women. In addition, the number of female health professionals is low, with female physicians constituting just 11 percent of all physicians, and the ratio of registered midwives per 10,000 people standing at only 0.5. These conditions are exacerbated by a poor referral system, a lack of communication between primary and secondary health care providers, an emigration of skilled workers, and internal obstacles faced by women in terms of enforcing their reproductive rights.

Alongside other vulnerable groups, pregnant women are particularly seriously affected by Israel's construction of the Wall in the West Bank that began in 2002. The Palestinian Ministry of Health estimated that 117,600 pregnant women, including 17,640 high-risk pregnant women, may not be able to access antenatal care, hospital delivery services and postnatal care [61]. As such, the dangers posed to women during pregnancy and whilst giving birth have increased drastically, indirectly contributing to the infliction of enormous psychological strain on women [60].

Many patients, including chronic and disabled patients, as well as health personnel and medicines, consequently have trouble reaching clinics. Forty-one primary health care clinics located in the West Bank will be isolated totally from the rest of other urban and rural centres. Labs, women and child health programmes, vaccinations, and health education have also been severely weakened, and 55% of clinics have difficulties procuring drugs and medical equipment.

It is estimated 80,000 Palestinians have difficulty accessing emergency care and curative medical services, a further 80,000 have trouble reaching hospitals, and 35,000 lack sufficient health care services. 6,000 more suffer deficiency in vaccination programmes, availability of general practitioner, preventive dentistry, and labs. Four communities in the Qalqiliya/Salfit area, Al-Za'im and Kalandia villages in Jerusalem, and Al-Walaja village in Bethlehem, 5,300 people in all, have no medical services whatsoever. Before the Wall was built, people in these areas could travel on back roads to bypass checkpoints and reach medical care, but this is now impossible [62].

External obstacles affecting women's health are compounded by the prevalence of socio-cultural and religious beliefs and practices based on the patriarchal system that, amongst other things, serve to restrict women's ability to obtain their reproductive and productive rights. Women's limited bargaining power within the household plays a significant role in the high fertility rates found in Palestine [63]. In addition, family and community attitudes often prevent women from receiving proper care during pregnancy and delivery. As a result, women rarely consider their own health as a priority, particularly in the context of high levels of poverty, where women seek care only in cases of serious complications or illnesses [64].

These attitudes have been exacerbated since September 2000. Restrictions on the freedom of movement by Israeli policies are matched by restrictions imposed on girls by their families, who become increasingly protective in order to avoid potential risk and harassment at checkpoints. This lies at the heart of rising school dropout rates amongst girls and women, particularly at the university level [65], and women's general disappearance from the public sphere. According to the UN, it is also directly related to increasing rates of early marriage, as families compel their daughters to marry at an early age rather than send them to school: *"Reports of increasing early marriage suggest a higher drop out rate past compulsory levels of education, eventually leading to worsening economic security and family health. Early marriage contributes to 46*

percent of the drop-out rate for female students, particularly at the secondary level, due to the limitation of compulsory". In this context, mobility restrictions placed on women under the patriarchal system are exacerbated by the security concerns above, related to Israel's military occupation of the Palestinian territory. As such, women face three-fold difficulties in accessing reproductive health services, in terms of gender, poverty and the occupation. Statistics on the number of women and infants who have died in childbirth at checkpoints highlight the serious impact the socio-political, religious and security situation has on women and children's health, on top of existing problems associated with poverty and underdevelopment.

4.2 Cardiovascular Diseases in Palestine

At this crucial junction of Palestine's health system transition, cardio-vascular diseases contribute a significant proportion of total deaths. Cardiovascular diseases and diabetes are extremely widespread. In 2006, heart disease was the first leading cause of death in the population [9]. Cerebrovascular disease was the third leading cause of death in the total population constituting 11.0% of total deaths, with rate (29.8% per 100,000 population), the third in males (9.9%) and the second in females (12.4%) [9]. Hypertensive disease was the eight leading cause of death in total population at 4.8% of total deaths, the ninth leading deaths in males and females (2.7% and 3.8%) of males and females deaths respectively.

Hypertension and dyslipidaemia, although common, are inadequately detected and treated. Tobacco consumption among Palestinians is common, especially among the poor and related cancer account for a large proportion of all cancers.

Demographic and socioeconomic factors are speeding up the health transition, with sharp escalation of cardiovascular disease burdens expected over the next ten years. One of the challenges, however, is the availability of data that could estimate the overall prevalence of cardiovascular diseases, hypertension or diabetes mellitus. Information is obtained from mortality data through the different health centres and the current system counts only the visits of the patients to these centres, hence not reflecting the real prevalence or incidence. Due to the lack of a computerized system, classification by age and gender or any information on disabilities resulting from any of the chronic diseases are not available.

Chapter 5
LITERATURE REVIEW AND DEVELOPMENT OF CONCEPTUAL FRAMEWORK

The literature review was carried out at two distinct times, and in two different phases. The first phase was carried out during the preparation phase in 1997 which was updated in 2006/2007, and the second phase, was carried out after the data collection and during the final write-up.

In the first phase, Popline, Medline and Pubmed were the main literature databases searched; the WHO website was also used and suggestions from key informants were followed up.

In the second phase, the same sources were used, as well as Embase, the Cochrane collaboration, CAB direct, Eldis and Web of Knowledge. The last of these was also used to follow up on citations.

During both phases, the following keywords were used:

Reproductive history, gravidity, parity, age at first birth, coronary heart disease, CHD risk factors, lipids and lipoproteins, obesity, body mass index, waist-hip ratio, waist circumference, blood pressure, diabetes, metabolic syndrome and Framingham risk score. The geographical context (Palestine, Middle East, Arab countries etc) and other generic descriptors, such as women, old age, adult, etc were also applied in appropriate combinations. MESH terms based on these keywords were also applied. The terms applied are listed in Appendix 1.

Articles were inspected on the basis of titles and abstracts. For relevant articles, the full text was obtained and was included in the review. The results are reported in sections, as presented in the review chapter below.

5.1 Cardiovascular Diseases and Risk Factors

This first chapter of the literature review discusses the major classical risk factors for coronary heart disease and responds to the question "why women are special"?

According to the WHO report [66], an estimated 16.7 millions, or 29.2% of total global deaths, are due to the various forms of cardiovascular disease (CVD), including coronary (or ischaemic) heart disease (heart attack), cerebrovascular disease (stroke),

hypertension (high blood pressure), heart failure and rheumatic heart disease. Many of these CVDs are preventable by ensuring needed action on the major primary risk factors: unhealthy diet, physical inactivity, and smoking. More than 50% of the deaths and disability from heart disease and strokes, which together kill more than 12 million people each year, can be prevented by a combination of simple, cost-effective national efforts and individual actions to reduce major risk factors such as high blood pressure, high cholesterol, obesity and smoking [66].

These risk factors are no longer diseases of the developed world; some 80% of all CVD deaths worldwide took place in developing, low and middle-income countries, while these countries also accounted for 86% of the global CVD disease burden. It is estimated that by 2010, CVD will be the leading cause of death in developing countries [66].

Of the 16.7 million deaths from cardiovascular diseases (CVDs) every year, 7.2 million are due to ischemic heart disease, 5.5 million to cerebrovascular disease, and an additional 3.9 million to hypertensive and other heart conditions. CVD affects people in their mid-life years, thus undermining the socioeconomic development, not only of affected individuals, but families and nations [66]. Lower socioeconomic groups generally have a greater prevalence of risk factors, diseases and mortality in developed countries, and a similar pattern is emerging as the CVD epidemic matures in developing countries. In 2005, an estimated 17.5 million people died from CVD, representing 30% of global deaths [67].

This rise in CVDs reflects a significant change in diet habits, physical activity levels, and tobacco consumption worldwide as a result of industrialization, urbanization, economic development and food market globalization. People are consuming a more energy-dense, nutrient-poor diet and are less physically active. Imbalanced nutrition, reduced physical activity and increased tobacco consumption are the key lifestyle factors. High blood pressure, high blood cholesterol, overweight and obesity - and the chronic disease of type II diabetes - are among the major biological risk factors. Unhealthy dietary practices include high consumption of saturated fats, salt and refined carbohydrates, and low consumption of fruits and vegetables. When risk factors are combined, risk for CVD can increase. These risk factors tend to cluster and when they are combined risk for CVD can increase and can lead to disability and death.

5.2 Risk factors for CVD

There are a variety of risk factors that contribute to CVD morbidity and mortality. Through extensive research, many of these risk factors for CVD have been identified and are well documented and understood. Each of these risk factors can be categorized as preventable (those over which the individual has control) or non-preventable (those over which the individual has no control) as detailed in Table 5-1.

Table 5-1: Preventable and Non-preventable Risk Factors

Preventable Risk Factors	Non-preventable Risk Factors
Type II diabetes	Increased age
High blood cholesterol	Gender
High blood pressure	Race/ethnicity
Lack of physical activity	Family history
Overweight and obesity	
Unhealthy eating	
Smoking	

Fortunately, one can assume that research has identified almost all of the risk factors for CVD and has shown that most are modifiable through apparently simple lifestyle choices. While extensive efforts have been made in recent decades to improve these risk factors, many of these efforts have not been successful.

5.3 Coronary Heart Disease

This part of the literature review will focus on Coronary Heart Disease (CHD) and its associated risk factors especially those related to women. Coronary heart disease has been defined as a disorder of cardiac function due to an imbalance between myocardial function and the capacity of the coronary blood vessels to supply sufficient flow (to the heart muscles) for normal function [68]. Clinical syndromes related to coronary heart disease are angina pectoris, myocardial infarction (non-fatal and fatal), and sudden cardiac death [68].

Angina is the most common form of presentation among women with CHD [69]. While heart attacks (myocardial infarction) are less common among women than heart attacks in men, painless heart attacks are common in women, particularly in old ages [70]. If world-wide proportions are similar to those in the United States, approximately 40 percent of CHD presents as angina pectoris, 40 percent as myocardial infarction, and 20 percent results in sudden cardiac death [69].

Although the rates for CHD are declining in North America and Western Europe at the time the study was conceived, It is still unclear how much of the decline is due to a reduction in the incidence of disease and how much is due to improved survival [71]. Yet CHD remains the major cause of disability and death in women [72]. In the United Kingdom, coronary heart disease is the single leading cause of death among women above and below the age of 65 years [73] [74]. It accounts for over 40% of deaths in women at all ages [74]. Little is known about the distribution of CVD risk factors and their control in women [74]. In a study conducted by Lawlor et al on geographical variation in CVD risk factors and their control in older British women, found that although geographical variation in CVD is explained to some extent by differences in major risk factors and/or socioeconomic factors and health services utilization, some geographical variation remained even after adjustment for these factors which required further explanation [74]. This is not the case for Eastern Europe, where CHD rates have increased steadily without evidence of stabilization or decline [75] [76] [77].

Rates in the developing world are much less documented. It has been speculated that by the year 2000-2015, CHD will increase sharply and will be the leading cause of death for many developing countries. [78] [69] [79]

5.4 Major Classical Risk Factors for CHD

The major classic risk factors for coronary heart disease are the same for women as for men. Smoking, high blood cholesterol and hypertension all predict CHD in women but, for any given level, constitute a much smaller risk for women than for men [80]. However, among older ages, the prevalence of these classical risk factors is higher among women than among men [81]. At younger ages, women have lower coronary heart disease mortality than men, as women may be biologically more resistant to CHD with protection from higher levels of HDL-C and oestrogen, but the sex difference reduces after about age 50 years [82]. This hypothesis stemmed from the fact that male to female ratio for fatal CHD is consistently around 2:1 in various countries with different life styles and rates for heart disease. This sex difference in CHD incidence persists after taking into account common CHD risk factors [83]. Another hypothesis lead by Lawlor et al showed that secular, geographical and age related trends, highlight the importance of environmental factors in determining sex differences in CHD occurrence and which could not be explained solely by a cardio protective effect of oestrogen in women [84]. However, the underlying mechanisms for these associations

remain unclear, but plausibly include genetic, biological, environmental and socioeconomic factors acting along the life course [80]. It is interesting to note that biologically the classic risk factors confer the same magnitude of risk in relative terms. Thus a woman who smokes, or who has a high blood cholesterol level, has a greater risk of CHD than a woman who does not, and the proportional increase in this risk is the same as with men [82]. Other important risk factors in women include obesity and diabetes.

5.4.1 Smoking

In women, smoking has been shown to be a risk factor for CHD, and its adverse effect persists into older age [72] [85]. The effect of smoking on CHD risk is dose-dependent [81]. Premenopausal women who smoke have three times the risk of heart attack of non-smokers, and women who smoke more than 40 cigarettes a day increase their risk 20-fold [86]. Cigarette smoking is inversely associated with low socio-economic status, high educational level and income in both men and women [81].

5.4.2 Cholesterol

Total cholesterol rises with age in both men and women. Women have lower cholesterol value at younger ages, but a sharp rise occurs in the fifth decade, so that from age 50 onwards the average cholesterol level in women is higher than in men. [72] [87, 88]

5.4.3 Low Density Lipoprotein Cholesterol (LDL-C)

Levels of LDL-C follow a similar pattern with age to that of total cholesterol, rising with age in both sexes during adult life. LDL-C levels are consistently lower in women than in men until about the age of 50, when a cross-over occurs [89] [88].

5.4.4 High Density Lipoprotein Cholesterol (HDL-C)

Average levels of HDL-C are consistently higher in women than in men, throughout adult life, although this sex difference is reduced after middle age [89] [88]. HDL-C inversely predicts CHD in both middle-aged men and women, and in older women but less convincingly in older men [72].

5.4.5 Triglycerides

Triglycerides levels rise with age in women, although women's average triglycerides levels are consistently lower than those in men at all ages [89]. The sex difference is most marked in middle age and disappears during the later years of life [90] [89].

In both women and men, the risk of CHD increases as the level of total cholesterol rises [89]. The relation between the cholesterol fractions and CHD risk is stronger, particularly for HDL-C [89]. HDL-C is inversely and independently associated with CHD risk: the higher the HDL-C level, the lower the CHD risk. However the association of HDL-C with CHD risk is twice as strong in women aged over 50 years [89]. LDL-C is positively associated with the risk of CHD: the higher the LDL-C level, the higher the risk of CHD. The relationship between triglyceride and CHD risk is less clear, and it is uncertain whether there is a sex difference in this relationship [89].

5.4.6 Blood Pressure

In most populations, blood pressure rises with age in both men and women [72]. Systolic pressure rises throughout life while diastolic pressure tends to plateau around the sixth decade [72]. At younger ages, blood pressure in women is lower than in men, but after the menopause the rate of rise of systolic pressure with age is greater in women than men, leading to a higher prevalence of hypertension in older women [72]. Several observational studies in women have demonstrated the importance of both systolic and diastolic pressure in predicting CHD [91] [92] [93]. Although at all ages the risk is lower for women compared to men, the relative risk associated with a particular level of blood pressure is the same in women as in men [72] [80].

5.4.7 Diabetes

Diabetes imposes a greater risk of CHD in women than in men [72] [94]. The impact of diabetes on CHD in women is considerable, with relative risks of up to fivefold compared with non-diabetic women [95] [96] [97]. A meta-analysis of prospective cohort studies found that diabetes had a greater impact in women than men (relative risk 2.54 (95% CI: 2.08- 3.09) in women and 1.76 (95% CI: 1.51-2.05) in men, p= 0.004 comparison between women and men [98]. Diabetic women seem to lose protection from CHD as a result of the metabolic disturbances associated with non-insulin dependant diabetes mellitus [99]. It is possible that a high waist to hip ratio increases the likelihood of diabetes and also of CHD. McKeigue et al [100], showed that the insulin

resistance syndrome, associated with a striking tendency to central obesity in South Asian women and men, is the most plausible explanation for their high CHD mortality. Women with a higher waist to hip ratio have increased risk of impaired glucose tolerance and adult onset diabetes. In addition, total cholesterol and triglycerides increase and HDL-C levels decrease compared to non-diabetic women [81].

5.4.8 Obesity

Obesity is also associated with an increased risk of CHD, and sex differences in body fat distribution may partly explain the differences in CHD risk [81] [99]. Body fat distribution appears to be more significant than body weight with regard to CHD risk [2] [101]. Although obesity measured by BMI, has been associated with CHD risk in women [102], abdominal or central obesity (male fat pattern), appears to be more powerful CHD risk factor for women [103] [104]. The distribution of body fat is recognized as a contributing factor in the development of CHD, independent of relative body weight. There are links between central adiposity, insulin resistance, raised triglycerides and decreased HDL-C which may relate to CHD risk. The male pattern of obesity, with a high waist to hip ratio, is associated with higher risk of CHD than the female pattern of lower waist to hip ratio, which may partly explain the sex differences in CHD. It has been suggested that oestrogen protects younger women from CHD via an influence on body fat distribution [105]. The Gothenburg study in Sweden [106], found that differences in blood pressure, smoking, blood cholesterol and BMI only explained a small part of the sex difference in CHD rates, but when waist to hip ratio was also considered, the sex difference in CHD risk almost disappeared. In a cross sectional survey using data from the British regional heart study, Lawlor et al [101] suggested that sex differences in lifestyle risk factors (alcohol consumption, smoking and physical inactivity) do not explain sex differences in CHD occurrence, although they increase waist to hip ratio. In this same study, Lawlor et al. suggested an important role for abdominal obesity in explaining sex differences in CHD risk. Adjustment for waist to hip ratio removed the sex differences in CHD occurrence [101]. Therefore, the study concluded that sex differences in body fat distribution may explain sex differences in arterial atherosclerosis. Body fat distribution, or factors closely related to it, may thus be part of the explanation for sex differences in CHD.

Other factors may contribute to the increased risk of CHD such as low socio-economic status, stress, lack of physical activity and high cholesterol, high fat diet among both women and men.

5.5 Are Women Special?

Women may have additional risk factors for CHD not found in men, namely those related to reproductive function: pregnancy, hysterectomy, menopause, and use of steroid hormones. Although childbearing is a major biological and social event in the lives of most women, little is known about the relationship between the pattern of childbearing and total mortality and morbidity [107]. A women's risk of developing various diseases is altered during the course of pregnancy and in the immediate postpartum period [108]. It has been very well documented that pregnancy confers long term protection against certain cancers such as breast and ovary, but its long term effect on other conditions such as CHD has been less extensively studied [7].

Among women of reproductive age, the atherosclerotic process is lessened, as compared with men of the same age range, possibly due to an influence of circulating oestrogen on the incorporation of LDL-C into atherosclerotic plaques [2]. Therefore, women seem to be less susceptible to CHD at least until perimenopause. However, Lawlor et al [84], does not totally agree with this hypothesis. In an attempt to examine secular trends and geographical variations in sex differences in CHD mortality and how these relate to distributions in risk factors, Lawlor et al found that a protective effect of oestrogen alone could not explain the variation over time and between countries among the sex differences in mortality from CHD. They suggested that these secular and geographical trends indicate that sex differences in mortality from CHD are driven primarily by environmental factors. In an attempt to explain why women develop acute MI later than men, the INTERHEART study [109] a global case-control study including participants from 52 developed and developing countries, investigated if differences in risk factor distributions exist between women and men across various age categories. They found that women experience their first myocardial infarction (MI) on average ten years later than men in all regions of the world. Nine modifiable risk factors are associated with incidence of MI and explain more than 90% of the population attributable risks of acute MI among women and men from all regions of the world. Similar risk factor associations with MI are present in women and men for abnormal lipids, current smoking, abdominal obesity, dietary intake and psychosocial stress factors. However, risk factor MI associations for hypertension, diabetes, physical activity, alcohol use, and

former smoking differ between sexes. They also found that these associations are stronger in younger individuals both in women and men. The younger age of onset of acute MI in men, is largely explained by higher levels of risk factors including abnormal lipids, and smoking before the age of 60 years. Therefore they concluded from the INERHEART data, that the lower MI burden among women at younger ages is largely explained by a lower risk factor burden. The reasons why the risk factors are lower in women at younger ages compared to men are still unclear and continue to be an area of controversy.

Identification of the factors responsible for sex differences in occurrence of CHD would have important public health implication in identifying preventive strategies, particularly in countries where rates of CHD are currently increasing.

Reproductive history, is generally thought of as beginning with menarche and ending at menopause [7]. This time period may be punctuated by timing and number of pregnancies and their outcomes: live births, stillbirths, miscarriages, and breast feeding. The full description also includes ages at menarche and menopause, regularity of menstruation, fertility, gynaecological or obstetric problems, and contraceptive use. For the purpose of this study parity was used as the exposure variable. Parity is defined as the number of offspring the woman has born. It is contrasted with gravidity which refers to the number of pregnancies regardless of outcome.

5.6 Parity and Coronary Heart Disease Risk Factors

The second part of the literature review covers the epidemiological association between high gravidity, high parity and early age at first birth and increasing risk of coronary heart disease in women, as well as likely biological and behavioural mechanisms between reproduction and coronary heart disease. Epidemiological research relating reproductive history and coronary heart disease risk has used population, cohort, cross-sectional and case-control studies.

Section 5.6.1 provides a review of epidemiological evidence relating high gravidity, high parity and early age at first birth and CHD morbidity and mortality in women and discusses some of the methodological difficulties involved in interpreting the results from such studies.

Section 5.7 discusses links between reproductive history and known risk factors. These include studies of gravidity, parity and age at first birth as the exposure variables and obesity, lipid levels, diabetes and hypertension as the outcome variables.

Section 5.8 discusses parity with the metabolic syndrome as an outcome variable.

Section 5.9 discusses proposed mechanisms for the association between gravidity/parity and CHD risk among women.

5.6.1 Reproductive History and Coronary Heart Disease (CHD) Morbidity and Mortality

An increased risk of CHD morbidity and mortality among women with high gravidity, high parity, and early age at first pregnancy or live birth was found in most studies in which these relationships were examined (Tables 5-2, 5-3 and 5-4). Of the eight published cohort studies in women [107, 110-115], all except for the Nurses' Health Study [116], showed small but consistent associations between gravidity/parity and an increased risk of CHD. The magnitude of the relative risk, which must depend on which parity groups are compared as well as other study-specific factors, is of the order of 1.2-2.5. However, only three studies - the Framingham [110], the NHEFS [110], and the Norwegian study [113] - showed statistically significant results after adjustment for socio-economic status and other confounders (Table 5-2). The adjusted relative risks for these studies were 1.7, 1.9, and 1.2 respectively, comparing nulligravid/nulliparous women to those of 6+ and 5+ pregnancies / child births. The Nurses' Health Study showed an adjusted relative risk of 1.2, 95% CI (0.8-1.8) but this was not significant [116]. Steenland et al showed an increase of 1.18 in the risk, 95% CI (1.04-1.34), for those women with six or more live births adjusting for age only. But when a number of CHD risk factors were included as confounders, no increased trend in heart disease with increased parity was observed [115].

Six of eleven case-control studies [108, 117-122] showed increases in CHD risk with gravidity/parity in the order of 1.5-1.8, while five studies [123-127] have shown negative associations. Only Palmer et al demonstrated statistical significance after adjusting for many variables [117] (Table 5-3). The adjusted relative risk was 1.8 for comparing parous 1+ to nulliparous and 1.4 for comparing para 5+ to para 1-4. Beral found a 20% increase in mortality from CHD among parous women compared to nulliparous.

A significant increase in risk of CHD morbidity and mortality has been reported for age at first live birth less than 20 years, and to a lesser extent with age at first pregnancy less than 20 years. Relative risk estimates from five case-control studies [117, 118, 122, 124, 128], range from 1.7-3.4. The association was evident in both younger and middle-aged women, and was not explained by allowance for several identified potential confounding factors.

A nearly 3-fold increase in relative risk (2.7) was observed in studies where early age at first live birth and high parity (5+ children) were combined [117] (Table 5-4). This suggests that high parity and early age at first birth are independent risk factors for CHD. However, the one cohort study of Colditz et al, did not show an increased risk (RR = 0.6) for high parity and early age at first live birth [116].

Two of the three cross sectional studies showed J-shaped and a U-shaped relationships between the number of children and coronary heart disease and carotid Intima-Media Thickness (IMT) respectively [8, 129]. Lawlor et al found a positive association between parity and CHD for those with at least 2 children, and each additional child increased the age-adjusted odds of CHD by 30% (OR: 1.30; 95% CI: 1.17-1.44) for women. Adjustment for obesity and the metabolic risk factors attenuated the association between greater number of children and CHD in both sexes, although in women some association remains [8]. In both women and men, there was a J-shaped associations between number of children and age-adjusted prevalent CHD, with the prevalence being lowest among those with 2 children [8]. Wolff et al [129] found a U-shaped association between the number of children (from 0-≥ 4) and mean and maximum IMT. Nulliparity and higher number of children are associated with increased carotid IMT. Nulliparous women had the highest age-adjusted mean (0.81 mm [95% CI, 0.78-0.84]) and maximum IMT (1.04 mm [95% CI, 1.00-1.09]), whereas women with single parity had the lowest (mean IMT, 0.73 [95% CI, 0.72-0.74]; maximum IMT, 0.91 mm [95% CI, 0.89 to 0.93]). Stepwise multivariate adjustment for socio-economic factors, lifestyle variables and biological variables attenuated the magnitude of this association yet significance remained [129].

The Rotterdam study [130] showed a significant association between parity and risk of carotid artery plaques in elderly women where parous women compared to nulliparous women had 36% (1.09-1.71) greater risk of carotid atherosclerosis, rising to 64% (1.19-2.27) in women with ≥ 4 children. Adjustment for known cardiovascular risk factors,

including insulin resistance and current lipid levels, did not diminish the magnitude of the association [130].

Most of the studies that have considered the association between number of children and CHD risk among women, have found increasing disease, mortality and increased carotid intima-media thickness with increasing number of children as mentioned above. Biological mechanisms were proposed including pregnancy lowering lifetime oestrogen exposure and pregnancy resulting in permanent changes to lipid and carbohydrate metabolism.

Some authors such as Lawlor et al [8] and Hardy et al [131], proposed an alternative explanation which says that that social and behavioural factors associated with child rearing and family life might underlie any association between number of children and CHD risk factors). In order to prove their explanation, they have included men as a way to assess the relative contribution of social and biological factors when studying the association between number of children and CHD risk. Lawlor et al concluded that the association between number of children beyond two and increased CHD and risk factors could be explained by socio-economic factors in men but could not explain the same association in women and therefore concluded that the association among women is explained by biological factors [8]. Hardy et al found that although BMI, WHR and type II diabetes showed a linear increasing trend with increasing number of children in women compared to men, yet these associations were largely explained by adjustment for behavioural and lifestyle factors. They found that women with four or more children were more likely to be smokers, inactive and come from manual social classes in childhood and adulthood [131].

The largest cohort, cross-sectional and case-control studies showed significant positive associations. Conflicting findings and some of the differences arise from the limitation of methods used in some of these studies. In the following sections, we will shed light on some of the methodological issues related to the association investigated.

5.6.1.1 Cohort studies

In cohort studies, lack of power may possibly differentiate between studies showing positive results and those that are not. Three factors, age of women, length of follow-up and the range of outcome studied all contribute to the results.

Age of women participating in the studies: The age of women studied ranges from 16-84 years. The moderate but consistent association was seen mostly in the older aged cohorts (≥50 years), an age range by which more women develop CHD (Table 5-2). Young women <50 years old, are known to be protected from CHD as a result of oestrogen action. The inclusion of young women, who experienced a low rate of CHD, might have masked an association between high gravidity/parity and CHD among older women by reducing the likelihood of a positive association. Alternatively, parity may act differently in pre-menopausal women.

Years of follow-up: The longer the follow-up period, the greater the number of CHD events in the study. Studies with long follow-up periods (12-28 years), showed positive associations compared to studies with shorter follow-up period (6 years) (Table 5-2).

Inclusion of angina in defining the outcome: Two of the three studies that showed a positive association after adjusting for multiple confounders (Table 5-2, the Framingham study and the NHEFS), included angina as a component of CHD end points. This led to an increase in the number of women who had a positive outcome. Exclusion of angina from the definition of CHD diminished the strength of the association in the Framingham study (rate ratio for women with 6+ pregnancies, 1.4; 95% CI, 0.9-2.2) but had no effect on the association in the NHEFS (rate ratio for women with 6+ pregnancies, 1.3; 95% CI, 1.0-1.7). This could be because half the cases of CHD among women in the Framingham study were due to angina, whereas this was only 14% in the NHEFS. An alternative explanation is the failure to adjust for confounders and mediators.

Confounders and Mediators: Most likely confounding and mediating factors include age, CHD risk factors, social class and life style variables. Most of the cohort studies have controlled for either CHD risk factors or social class and life style variables or all of them combined. Studies that extensively adjusted for CHD risk factors, socio-economic status and life style variables showed a positive association [110] (Table 5-2, Ness et al, the Framingham study and the NHEFS). Studies that managed to control for measured CHD risk factors at baseline [110] showed a positive association compared to others where information on CHD risk factors was based on self reports (the Nurses' Health Study) [116]. All these studies suggest that parity is an independent risk factor for CHD even after controlling for confounders.

A confounder is a variable that distorts the association or the relationship between an exposure and an outcome and must be a risk factor for both the outcome and the exposure, while not being on the causal path between the two. Therefore a confounder does diminish or eliminate the importance of parity related risk. Not allowing for a confounder can lead to an erroneous assessment of the role of the risk factor on account of confounding bias. Not every factor that is associated with both the exposure and the outcome is a confounding variable. A mediator is also associated with outcome and risk factor but may be part of the causal chain between them. Therefore finding a mediator doe not diminish the importance of parity as a risk factor, it just assists in explaining parity related risk. Allowing for a mediator can help understand the risk factor outcome relationship but is not needed to establish that the risk factor is a genuine correlate. In some of the papers reviewed the distinction between confounders and mediators is not always made when adjustments are made.

Men with high parity and CHD morbidity: The relation between the number of children and risk of CHD in men has been explored in two cohort studies [112, 114] and one cross-sectional study [8] for two reasons: first, to explore potential risk factors in men; and second, to evaluate the role of potential mediators of this association in women [8, 112, 114], e.g. biological plausibility via pregnancy vs. exogenous factors such as stress and life-style factors. Men with 6+ children (Table 5-2) showed a slight increase in the relative risk compared to those with no children in the Framingham study, adjusted relative risk, RR =1.2 (0.8-1.8), and men with 4+ children compared to none [114]. The Dekker and Schouten study [112] showed a relative risk of RR= 1.6 (0.9-2.6). In Lawlor et al each additional child, for those with at least two children, increased the age-adjusted odds ratio of CHD by 12% for men (odds ratio, 1.12; 95% CI, 1.02-1.22) compared to 30% (OR: 1.30; 95% CI: 1.17-1.44) for women. Adjustment for obesity and the metabolic risk factors attenuated the association between greater number of children and CHD in both sexes, although in women some association remain [8]. This association among men with high parity and CHD morbidity and mortality did not attain significance levels but was similar to results for women in Dekker and Schouten study, which suggests some impact of non-biological factors. The NHEFS, on the other hand, showed no association (RR 0.7 [0.4-1.3]) [114].

The consistency of the results among different studies using various adjustments for socio-economic status and lifestyle variables suggests that the association between gravidity/parity and CHD cannot be explained entirely by the factors mentioned above,

although they may make an important contribution to the association among women [114]. It suggests that (biological plausibility) the process of being pregnant and therefore having children has an independent impact on the risk of CHD. But there is a room for social or emotional factors associated with raising up children that may differentially affect men and women [8, 132]. The lack of significant association in men contrasts with the previous positive association found between pregnancy/parity and CHD in women, independent of other known risk factors.

5.6.1.2 Case-control studies and cross-sectional studies

Conflicting findings among the different case-control studies may have resulted from the following sources:

Age of women participating in the studies: Ages of women studied varied greatly among the case-control studies and ranged from 16-84 years. It is interesting to note that the case-control studies that failed to show an association between high gravidity/parity and CHD are those studies that included women who were less than 50 years of age (Table 5-3), an age range in which few women develop CHD. Studies that showed positive associations included women of peri- or postmenopausal age, or women of all ages.

Sample size: Studies with large sample sizes (Table 5-3) showed positive association, especially when different categories of the exposure and the outcome have enough cases to allow for associations to be seen. In general large sample sized studies will have greater power to detect small associations compared to studies with smaller sample size.

Measurement of exposure: Exposure has been measured by a questionnaire and was stratified to different categories. Some studies measured parity, others gravidity, pregnancy loss, age at first pregnancy/birth or more than one exposure combined (Tables 5-3 and 5-4). Age at first pregnancy has been used many times to mean age at first birth and vice versa, although the two terms give different end products. Women might have many abortions before they can have their first live birth which might affect the association between parity and CHD risk (e.g. Beard et al 1984 used the term parity as an exposure but in the analyses, the authors used the number of pregnancies to compare 4+ pregnancies vs. nulligravid).

Comparison of the risks occurring from each of these exposures discussed above, may be impeded by the inaccuracy of patient's recall [7]. Pregnancy losses and thereby

gravidity are less likely to be fully recalled compared to parity. This applies to all studies using gravidity as an exposure in both case-control and cohort studies.

Definition of exposure: Definition of the cut-off points for the exposure has not been consistent throughout the studies. Some defined high parity/gravidity as having 6+ children/pregnancies, or 5+ children/pregnancies or 4+ children/pregnancies. Some studies only mentioned high parity/gravity without further categorization, whereas others used increase in risk per one child [8, 130], which makes it difficult to compare (Table 5-3).

Most studies have used nulliparous or nulligravid women as the referent group. Nulliparous/nulligravid women were defined as married women with no children or never being pregnant, except for 3 studies (the Framingham, the NHEFS and Beard et al 1984 (Tables 5-2 and 5-3) where they included single in addition to married women in their definition. But when the single women were excluded from the analysis, the results did not change. In all these studies, clear explanations or definitions of nulliparous/ nulligravid women (other than being married with no children or never being pregnant) was missing. It remains difficult to know if these women are nulliparous/nulligravid because they have an early menopause or married at a later age? Are they infertile women? Are they single or divorced? The answer remains unclear. Different categories of nulliparity or nulligravidity may not have a uniform association with risk of CHD. This was clear in the Humphries et al study which showed that childless women in the Rotterdam study were socially well situated and deliberately childless [130], in contrast to the SHIP study by Wolff et al, where most women had grown up in the former East Germany, where childbearing was strongly encouraged and generously subsidized and where childless was hence uncommon [129]. Therefore the group of childless women was in the first case made up of well educated more affluent women, who are voluntarily childless, and for the second case was made up much more of women who for unknown reasons were incapable of getting children. With both group of women, the risk of IMT increased [129].

Definition of outcome: Definition of outcome varied among the studies. Some used CHD mortality [108, 126], while others used CHD morbidity. Among the CHD morbidity studies different end points were used. Some used angina, others used myocardial infarction, ischaemic heart disease, or a combination of all. Two studies have used sudden cardiac death [118, 122], but the sample size was small with low

power to detect associations. Two studies used Carotid Intima-media Thickness as an outcome [129, 130]. Using different definitions for the outcome makes comparison between studies a difficult task.

Definition of a positive relation between parity and CHD: The positive association in the studies reviewed has been defined in different ways. Some investigators consider that CHD is related to parity if the disease rates differ in the parous (regardless of the number of children the woman has) compared to nulliparous [118, 120, 127], whereas others look for a trend in risk with increasing numbers of pregnancies or live births [8, 117, 123, 124, 129, 130] (Table 5-3). Others have examined relationships between miscarriage and disease [119]. Marital status has been used as a proxy for parity in some studies, and the lower mortality of married compared to single women has been attributed to the different life style, working conditions and the beneficial effects of childbearing on health, or to selective factors leading women to marry [108, 122].

Controlling for confounders and mediators: Croft and Hannaford, found that women with 5+ pregnancies had a 1.8 increased risk of myocardial infarction before adjusting for social class and cigarette smoking. After adjustment, the relative risk was 0.9, suggesting confounders may well explain, or at least contribute to any association seen [123]. The control for confounding factors and mediators varied among the studies. Some studies controlled for mediators that could act on the causal pathway such as known CHD risk factors: hypertension, body mass index, cholesterol etc [117, 124], but others did not [118, 121, 122, 126, 127]. Some studies controlled for confounders such as socio-economic class [117, 123, 124], and others did not [108, 118, 122, 125]. For more details please see Table 5-3. Some controlled for both confounders and mediators such as socio-economic factors, lifestyle variables and metabolic risk factors [8, 129, 130]. In some of the cited literature, results are given with adjustment for both confounders and mediators, and there is a basic difficulty of interpretation when this occurs.

Selection of controls: Selection of controls is often an issue in case-control studies e.g. community controls vs. hospital controls. In the studies reviewed (Table 5-3), the choice of controls from either the community or the hospital did not seem to affect the association between gravidity/parity and CHD risk.

Age at first pregnancy/ live birth: Age at first pregnancy/live birth less than 20 years has shown to be an independent risk factor for CHD morbidity and mortality. All studies

showed significant association except for the Nurses' Health Study [116], where only 1% of the nurses had an age at first birth ≤ 19 years, and therefore if any effect for such an early age at first birth exists, the study design might not have been able to detect it. Alternatively, age at first birth might be confounded by socio-economic status. The study of Nurses is by definition looking at a cohort with similar socio-economic status and may be less confounded.

In summary, most of the prospective studies and the well designed and thought-out case-control studies have shown a consistent and significant association between multigravidity, multiparity and age at first live birth of less than 20 years with CHD morbidity and mortality. When results were adjusted for potential confounders and mediators, including social class, CHD risk factors, and life style variables, the relationships remained significant.

Table 5-2: Cohort Studies of Gravidity/Parity* and Coronary Heart Disease

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR†	95% CI‡	Comments
Ness et al 1993 USA Framingham Heart study [110]	Prospective cohort study of 2357 women who completed childbearing. Mean and median No. of pregnancies were 2.3 & 2. Years of follow up: 28 years	35-68	28	Multigravid 6+ Vs. nulligravid 0 0 1or 2 3-5 6+	Incident cases of coronary heart disease (CHD)	 1.0 1.1 1.1 1.6	 referent 0.9-1.4 0.9-1.4 1.1-2.2	Rates for CHD adjusted for age and educational level were higher in women with 6 or more pregnancies compared to women with no pregnancies
				0 1 or 2 3-5 6+		1 1.1 1.1 1.7	referent 0.9-1.5 0.9-1.4 1.2-2.4	Adjustment for age, educational level, and other CHD risk factors (BMI, systolic blood pressure, total cholesterol level, cigarette consumption, the presence of glucose intolerance, and the presence of left ventricular hypertrophy) did not alter the risk in women of the highest gravidity.

* Gravidity defined as number of pregnancies; Parity defined as number of live births.

† RR: adjusted relative risk

‡ CI: confidence interval

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR†	95% CI‡	Comments
Ness et al 1993 USA National Health Epidemiolo-gical Follow-up Study NHEFS [110]	Prospective cohort study of 2533 women who completed childbearing. Mean No of pregnancies was 3, median was 3. Years of follow up: 12 years	45-74	12	Multigravid 6+ vs. nulligravid	Incident cases of CHD	1.5 1.3 1.9	1.1-1.9 1.0-1.8 1.1-3.3	Adjusted for age and educational level Adjusted for age, educational level, BMI, systolic blood pressure, total cholesterol level, smoking status, and the presence of a history of diabetes Among women aged 45-64 years, there was a 90% increase in multigravid women as compared with nulligravid women after adjustment for the above mentioned CHD risk factors (BMI, SBP, T-cholesterol, smoking, and history of diabetes).
Green and Beral 1988 UK [111]	A population longitudinal study of 108,352 currently married women classified from the 1971 census up to 1981 according to their husband's social class	16-59	10	Multiparous 5+ vs. nulliparous Paraus <5 vs. nulliparous	Ischaemic heart disease mortality (IHD)	SMR* 1.25 0.99	0.93-1.64	Adjusted for age and social class. Mortality from IHD tended to rise with parity though the trends were not statistically significant. Women with five or more births had a 25% increase in risk. Nilliparous women and women with lower parity had SMR around the null value of one.

* SMR: Standardised Mortality Ratio

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR†	95% CI‡	Comments
Dekker and Schouten 1993 Holland [112]	Cohort prospective study of Dutch civil servants and their spouses, 1953 to 1981. 1200 married women	40-65	28	Multigravid 4+ vs. nulligravid	Mortality from CHD	1.4	0.6-3.3	Adjusted for age, systolic blood pressure, total serum cholesterol level, BMI, income level, and cigarette smoking
				Multiparity 4+ vs. nulliparous		2.5	1.0-5.8	Adjusted for the same CHD risk factors and social class.
	1048 husbands		28	4 + children vs. none	Mortality from CHD	1.6	0.9-2.6	Adjusted for the same CHD risk factors and social class.
Kvale et al 1994 Norway [113]	A population longitudinal study of 63090 Norwegian women 1961-1980	32-74	20	Parity: nulliparous to 5+	Ischeamic heart disease mortality	OR* 1.19	P 0.002	Adjusted for age, county, urban/rural place of residence and occupational group Moderate but highly significant positive trends of increasing mortality from IHD with increasing parity 5+ children, were observed in the older age group of the cohort ≥50, P-value for linear trend is 0.002.
Lund et al 1990 Norway [107]	A population cohort study with all currently married women at the 1970 Norwegian census, 1970-1985. (822593 women)	25-84	15	Nulliparous vs. parous	Total mortality	1.66	1.63-1.68	Adjusted for socio-economic group
				Nulliparous vs. parous 3		1.39	1.35-1.44	Increased total mortality in the nulliparous as well as among women with high parity was observed
				parous 6 vs. parous 3		1.07	1.01-1.14	
				Parous 10 vs. parous 3		1.48	1.22-1.79	
				Parous 3-4 vs. nulliparous		0.65	0.63-0.68	The lowest mortality was found for women with 3-4 children.

* OR: odds ratio

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR†	95% CI‡	Comments
Colditz et al 1987 USA Nurses' Health Study [116]	A prospective study of 119,963 US married registered nurses 1976-1982	30-55	6	Nulliparous vs. parous	Incident cases of non-fatal myocardial infarction Fatal MI	1.2	0.8-1.8	Adjusted for age and CHD risk factors. Among parous women there was no alteration in risk with increasing No. of births, P=0.4
Ness et al 1995 USA Framingham Heart Study [114]	Prospective cohort study of 1632 men	35-69	30	6+ children vs. no children	CHD incidence	1.2	0.8-1.8	Adjusted for age, BMI, serum total cholesterol, systolic blood pressure, current No. of cigarettes smoked per day, education, left ventricular hyper- trophy, and glucose intolerance.
NHEFS [114]	A cohort study of 2584 white men. 1982-84	35-74	3-5	6+ children vs. no children	CHD incidence	0.7	0.4-1.3	Adjusted for age BMI, serum total cholesterol, systolic blood pressure smoking status, self-reported diabetes mellitus, and educational status. No association between parity and CHD incidence among men

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR†	95% CI‡	Comments
Steenland K et al 1996 American cancer society [115]	A cohort study of 585,445 women from the American Cancer Society Survey. There were 4787 deaths from heart disease among these women during follow-up period from 1981-1989	30 years and older	12 years	Livebirths 1 vs none 2 vs none 3 vs none 4 vs none 5 vs none ≥ 6 vs none	Heart disease mortality	 0.95 0.89 0.82 0.94 0.98 0.94	 0.86-1.05 0.81-0.97 0.74-0.91 0.84-1.05 0.85-1.13 0.83-1.08	There was no increase in heart disease with parity when adjusted for age, BMI, t-chol, SBP, education, smoking and history of diabetes mellitus. All parous women had a lower risk than nulliparous women. When data was analyzed including age only as a confounder. When data was analyzed including age only as a confounder, there was an 18% increase risk for those with six or more livebirths RR 1.18, 95% CI (1.04-1.34).
NHANES data		45-74 years	8 years	Parity 0 1-2 3-5 ≥ 6	Heart disease 109 219 181 70	 1 1.15 1.16 1.36	 Referent 0.91-1.45 0.91-1.48 1.01-1.84	Elevated risk in women with six or more children was seen after adjustment for the same confounders.

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR[†]	95% CI[‡]	Comments
Humphries K, Westendorp I, et al 2001, The Rotherdam study The Netherlands [130]	A population-based study comprising of 2681 postmenopausal women aged 55 – 99 years who participated in the Rotherdam study	55 years and above		Parity vs. nulliparous	CVD risk factors			High parity was significantly associated with lower HDL-C levels and higher T-chol/HD-C ratio, higher glucose/insulin ratios, higher BMI, W/H ration, long after childbearing has ceased.
				Per child	Presence of carotid plagues	OR[*] 1.10	1.04-1.17	For every live birth, risk of carotid artery plaques increased by 10%, 95% CI (4%-17%)
				Parity ≥ 4 vs. parity 0		1.64	1.19-2.27	Parous women with ≥ 4 children have a 64% greater risk of carotid artery plaques compared to nulliparous women, adjusted for age, smoking status, socioeconomic status, hypertension, diastolic and systolic blood pressure, BMI, lipids and insulin/ glucose ratio.
					Mean IMT,[†] mm	Mean IMT		A trend of increased mean and maximum IMT was observed with increasing parity, and remained significant after adjustment for the above mentioned covariates (p=0.005, p=0.0001).
				0		0.75	0.73-0.77	
				1		0.74	0.72-0.76	
				2-3		0.77	0.76-0.79	
				≥ 4		0.81	0.77-0.84	
					Maximum IMT, mm	Max IMT		
				0		0.98	0.95-1.01	
				1		0.96	0.93-0.99	
				2-3		1.01	0.99-1.03	
				≥ 4		1.06	1.01-1.11	

[*] OR: Odds ratio
[†] IMT: Intima-Media Thickness

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR†	95% CI‡	Comments
Lawlor DA, Emberson, Ebrahim Shah, JR, et al 2003 UK [8]	A cross sectional study of 4286 women and 4252 men from 24 British towns. Among women: mean parity 2.3 Among men: Mean parity 2.2	60-79 years		Number of children (parity)	CHD risk factors. Reported CHD events.	OR* 1.30 1.12	1.17-1.44 for women 1.02-1.22 for men	Number of children was positively associated with BMI and WH ratio in both sexes. In women, number of children was associated with lower HDL-C, higher triglycerides and diabetes. A J-shaped association was found between number of children and age adjusted prevalent CHD. Each additional child beyond 2, increased the age-adjusted odds of CHD by 30% for women and by 12% for men. Adjustment for obesity and the metabolic risk factors attenuated the associations between greater number of children and CHD in both sexes, although in women some associations remained.

* OR: Odds Ratio.

Author(s) & Year	Study Design	Age Range (Years)	Years follow-up	Exposure	Outcome	RR†	95% CI‡	Comments
Wolff B, Volzke H, et al 2005 Study of Health in Pomerania Germany [129]	A cross sectional study of a sample of 1195 women withdrawn from the larger population study in West Pomerania, the Northeast Coastal Region of Germany	45-79 years		Number of children (parity) Parity 0 Parity 1 Parity 2 Parity 3 Parity ≥ 4 Parity 0 Parity 1 Parity 2 Parity 3 Parity ≥ 4	Mean and maximum age adjusted IMT*	Mean IMT 0.81 0.74 0.74 0.75 0.77 Max IMT 1.05 0.92 0.92 0.97 0.95	 0.78-0.84 0.71-0.74 0.73-0.75 0.73-0.77 0.74-0.80 1.0-1.10 0.89-0.95 0.90-0.95 0.94-1.00 0.91-0.99	A U shaped relationship existed between parity and age adjusted mean and maximum carotid IMT values. Women with 1 and 2 children exhibited the lowest mean as well as maximum carotid IMT values, whereas nulliparity and higher number of children (>2) were associated with higher IMT values. Stepwise multivariate adjustment for socioeconomic factors, lifestyle variables, and biological variables attenuated the magnitude of the association, yet significance remained. (P values for comparison with single parity as a reference group: P<0.001 for mean IMT and P<0.001 for max IMT).

* IMT: Intima-Media Thickness of the common carotid arteries.

Table 5-3: Case-Control Studies of Gravidity/Parity and Coronary Heart Disease

Study	Design	No and Subjects cases	Type of controls	Range (Years)	Exposure	Outcome	RR*	95% CI†	Comments
Beral V1985 UK [108]	A descriptive analyses of population statistics for married women who died in England and Wales between 1938-1960.	1163341 parous	Nulliparous baseline unexposed group	45-74	Parous vs. nulliparous	Overall mortality (all causes SMR)	SMR† 120	–	Significantly more risk of atherosclerotic heart death in parous women. Age adjusted mortality ratio
Palmer et al 1992 USA [117]	A case-control interview study on women in Massachusetts 1986-1990, median age was 60 years	858 hospital	858 neighbour-hood	45-69	Parous ≥1 vs. 0 nulliparous	First non-fatal MI‡	1.8	1.0-3.3	Adjusted for age. Cases were age matched with controls from same neighbourhood. Parity is a significant risk factor for MI
					Parity 5+ vs. parity 1-4		1.4	1.0-2.0	Adjusted for strata of age at first birth, education, smoking and occupation, hypertension, cholesterol, diabetes, family history, physical activity, BMI, alcohol consumption

* RR: adjusted relative risk; CI: confidence interval
† SMR: standardised mortality ratio
‡ MI: Myocardial Infarction

Study	Design	No and Subjects cases	Type of controls	Range (Years)	Exposure	Outcome	RR*	95% CI†	Comments
Beard et al 1984 USA [118]	A case-control study of reproductive history with coronary heart disease. 1960-1974	169 clinic based	338 clinic based	< 60	Gravidity 4+ vs. nulligravid	CHD incidence angina (n=95) & MI (n=59) & sudden unexpected death (n=15)	1.5	0.8-2.9	Matched for age, sex and year of diagnosis
					Gravidity 4+ vs. gravidity < 4		1.4	0.9-2.1	Non- significant higher risk for women with 4+ pregnancies compared to women with no pregnancies
Winkelstein et al 1958 USA [120]	A case-control study of women surviving MI	50 hospital	50 neighbour-hood	mean age= 64	Gravidity vs. nulligravidity	Non-fatal myocardial infarction	1.2	0.1-2.5	Adjusted for age. Cases had significantly more pregnancies than did the controls. Parity increased, abortions increased. Gravidity increased.
Winkelstein and Rakate 1964 USA [119]	A case-control study of women surviving CHD	59 hospital MI positive	64 hospital other admissions	50-80	Gravidity 5+ vs. Nulligravid	Non-fatal MI	P < 0.05	_	Adjusted for age and diabetes mellitus.
					Pregnancy loss		_	_	Women with a non-fatal MI had approximately twice as many pregnancy losses from stillbirths and abortions as did the controls, matched for age, race and social class

Study	Design	No and Subjects cases	Type of controls	Range (Years)	Exposure	Outcome	RR*	95% CI†	Comments
Mant et al 1987 UK [121]	A case-control study of myocardial infarction and angina pectoris in young women. 1968-1985	54 25 MI & 29 angina	216	25-39	Parity 3+ vs. nulliparous	Non-fatal MI and angina	_	_	Matched on age, date of entry into the cohort and smoking history A progressive increase in adjusted disease incidence with parity 0, 1-2, and 3+, but was only significant with angina, P < 0.02
Croft and Hannaford 1989 UK [133]	A nested case-control study carried out on cohort data collected during the Royal College Practitioners oral contraception Study. 1968-1969.	158 Hospital women using OC pills	474 Hospital women never used OC pills	20-60	Parity 5+ vs. nulliparous	First non-fatal MI	1.8 0.9	 0.3-2.6	Unadjusted relative risk, matched for age. Adjusted relative risk, no association with parity after controlling for cigarette smoking, socio-economic status and use of oral contraceptives.

Study	Design	No and Subjects cases	Type of controls	Range (Years)	Exposure	Outcome	RR*	95% CI†	Comments
La Vecchia et al 1987 Italy [124]	A case-control study of myocardial infarction in women	202 Hospital ICU admission	374 Hospital Acute hospital admission	23-54	Parity ≥ 3 vs. nulliparous	Non-fatal MI	1.81	0.82-4.00	Adjusted for diabetes hypertension, obesity, hyperlipidemia, geographic area, marital status, education, social class, cigarette smoking, alcohol and coffee consumption, age at menopause, family history of CHD, oral contraceptives and other female hormone use, and age. No consistent pattern of risk of MI with parity.
					Parity 1-2 vs. nulliparous		0.73	0.28-1.85	
Talbot et al 1989 USA [122]	A case-control study of reproductive history of ever married women, dying of SCD*	67 Death records	73 Neighbour-hood	25-64	Nulliparous vs. parous	SCD*	0.8	0.3-2.1	Odds ratio, adjusted for age ≤50 years
					Nulliparous vs. parous		6.9	1.3-32.8	Odds ratio, adjusted for age > 50 years No relationship was seen of nulliparity and SCD among women aged 50 years and younger. However among women over age 50, the effect was statistically significant.

* SCD: Sudden Cardiac Death.

Study	Design	No and Subjects cases	Type of controls	Range (Years)	Exposure	Outcome	RR*	95% CI†	Comments
Oliver et al 1974 UK [125]	A case-referent study of ischaemic heart disease in young women.	145 Angina 64 & MI 81 clinic based	general UK reference population	< 45	Parous vs. nulliparous	Non-fatal MI and angina	–	–	RR not shown. Adjusted for age, marital status, and year of admission by matching. Not a significant association
Mann and Inman 1975 UK [126]	A case-control study of death from myocardial in young women who uses oral contraceptives	219 general practice	219 general practice	< 50	Parous vs. nulliparous	Fatal MI	–	–	RR not shown .Matched for age. No significant difference between cases and controls at any age with regard to parity and death from MI.
Mann et al 1975 UK [127]	A case-control study of myocardial infarction in young women with special reference to oral contraceptive practice	63 hospital	189 hospital	< 45	Parous vs. nulliparous	Non-fatal MI	–	–	Matched for marital status, five-year age group and year of admission. No statistical significant differences were found between the cases and controls with respect to parity. The patients with MI tended to have fewer pregnancies, and belong to a higher socio-economic group. Cases tended to have fewer pregnancies.

Table 5-4: Studies of Age at First Birth and Coronary Heart Disease

Study	Design	No and Subjects cases	Type of controls	Range (Years)	Exposure	Outcome	RR*	95% CI†	Comments
Palmer et al 1992 USA [117]	A case-control study of reproductive factors and risk of myocardial infarction (MI) among women in Massachusetts	858 hospital	858 Neighbour-hood	45-69	Age at first birth < 20 vs. 20+	First non-fatal MI	1.7	1.1-2.6	Adjusted for smoking education and occupation
					Parity 5+ and age <20 vs. nulliparous and age 20+		2.7	1.3-5.6	Adjusted for socio-economic status (education, smoking and occupation)
La Vecchia at al 1987 Italy [124]	A case-control study of myocardial infarction in women	202 hospital	374 hospital	23-54	Age at first pregnancy <20 vs. nulligravid	Non-fatal MI	2.29 2.97	1.03-5.11 0.92-9.59	Adjusted for age. Multivariate analysis adjusted for parity age, diabetes, hypertension, obesity, hyperlipidemia, geographic area, marital status, education, social class, cigarette smoking, alcohol and coffee consumption age at enopause, family history of CHD oral contraceptives and other female hormone use
Rosenberg et al 1983 USA [128]	A case-control study of MI in women	255 hospital	802 hospital	25-49	Age at first pregnancy <20 and parity ≥5 vs. never pregnant (nulligravid)	Non-fatal MI	1.9	1.0-3.8	Controlling for age and cigarette smoking. The RR estimate didn't reach statistical significance at the 0.05 level

* RR: adjusted relative risk;
† CI: confidence interval

Study	Design	No and Subjects cases	Type of controls	Range (Years)	Exposure	Outcome	RR*	95% CI†	Comments
Beard et al 1984 USA [118]	A case-control study of women surviving MI	169 clinic based	338 clinic based	< 60	Age at first pregnancy <20 vs. nulligravid	CHD incidence angina (n=95)	2.5	1.2-5.3	Controlled for smoking, hypertension and elevated serum cholesterol controlled for age at diagnosis, smoking, diabetes and hypertension
					Age at first pregnancy <20 vs. age at first pregnancy 25+ or nulligravid	MI (n=59) sudden unexpected death (n=15)	1.9	0.7-5.6	
					Age at first pregnancy 20-24 vs. 25+ or nulligravid		1.8	1.1-3.3	Adjusted for age at diagnosis, smoking, diabetes and hypertension
Talbot et al 1989 USA [122]	A case-control study of reproductive history of ever married women dying of sudden cardiac death SCD	67 Death records	73 Neighbour-hood	25-64	Age at first birth <20 vs. ≥ 20	SCD	3.4	1.1-9.9	OR: Odds ratio, controlled for age. Sudden death cases were significantly more likely to deliver their first born child before the age of 20 compared to ever - married controls. 26.9% of cases gave birth before age 20 compared to 10.3% of controls
Colditz et al 1987 USA Nurses' Health study [116]	A prospective study of 119963 US married registered nurses who were free from CHD in 1976 and were followed through 1982			30-55	Age at first birth ≤19 vs. ≥30	Incident cases of non- fatal MI, Fatal MI	0.6	0.2-1.8	RR adjusted for age and CHD risk factors. No significant association between age at first birth and risk of CHD

5.7 Links between Parity and Coronary Heart Disease Risk Factors among Women

The evidence discussed above suggests that women with many pregnancies and live births have a modestly increased risk of developing coronary heart disease (tables 5-2 and 5-3). The ways in which parity lead to an increase in the risk of CHD in women is unclear, but plausible biologic pathways, including changes in adiposity [6, 134-138], blood glucose [110, 139] and lipid levels [140-142], which may occur during pregnancy or persist after reproduction has ceased, may exist[6-8]. The following sections will discuss the different plausible pathways and the mediating conditions on them.

5.7.1 Parity, Body Size and Body Fat Distribution

Obesity is a significant public health problem in many developed and developing countries. Each year an estimated 300.000 adults die of causes related to obesity [143]. The prevalence of overweight (Body Mass Index (BMI $\geq$ 25 kg/m2) among women is high in developed countries; 62% of women aged 20–74 years in the United States of America (USA) are overweight [144]. And in developing countries, the prevalence of overweight among childbearing age women (15–49 years) is highest in the Middle East and North Africa, estimated at 45.9%, followed closely by Latin America and the Caribbean at 42.5% and 42.1% in Central Europe [145]. Excess body fat among older women has been linked to the development of type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, some cancers, osteoarthritis, and all cause mortality [7, 104, 146-151]. This high prevalence rate of overweight and obesity has major implications for any nation's health care system and the population quality of life [152].

When researching overweight and obesity among women, it is important to note that the female body undergoes changes in fat distribution during the different phases of reproductive life. This has led to the focus on reproductive history as a predictor for obesity and regional fat distribution. And because genetics could partially determine fat distribution, factors associated with differential deposition of fat in the abdomen versus the gluteal region are not well understood. However, Kaye et al and Bjorkelund et al, found that certain lifestyle and reproductive factors were cross-sectionally associated with body fat distribution in women [6, 134]. Rodin and Heliovaara have also identified

parity as a risk factor not only for increased weight but also for abdominal adiposity indicated by increased waist to hip ratio (WHR) [135, 153].

Lately, emphasis has been put upon the location of adipose tissue as a risk factor for cardiovascular disease and premature death (deposition of fat on trunk rather than on the hips or limbs, intra abdominal adipose tissue) rather than adiposity per se [154, 155]. In both men and women, abdominal adiposity, measured as an increased W/H ratio and/or increased WC, is a strong risk factor for coronary heart disease and overall mortality.

Moreover, female hormonal secretion in regular menstruation, parity and lactation all influence fat cell numbers and sizes as well as the location of regional fat depots [6, 134, 156] and levels of serum lipids [140].

The first period of major hormonal changes in women is menarche, which is known to be affected by body fat stores [6]. Although early menarche might indirectly influence parity via a longer total fertile period, and thus possibly influence subsequent adiposity, it can also act as a situation where adiposity influences reproduction by decreasing fertility. Also, reproduction can also affect adiposity as it is widely asserted that pregnancy is a major contributor to permanent weight gain in women and that the higher prevalence of overweight in women compared to men is partly due to child bearing [134, 153, 157-160].

Long term postpartum weight retention has been identified by many investigators as a cause of overweight and obesity. Table 5-5 summarises findings of studies that examined the association between body size, body fat distribution and parity among women of childbearing and beyond childbearing age. All studies on women of child bearing age have shown that postpartum weight retention significantly contributes to the development of overweight and obesity. And greater numbers of live births are associated with greater postpartum body size [134, 153, 157, 160-164]. The risk factors for this long term weight retention includes high pre-conceptual weight, excessive gestational weight gain, frequent reproductive cycles, race (white vs. black women) and lower levels of education [152, 165].

During pregnancy an average of 3.5 - 4 kilograms of maternal fat tissue accumulates preferentially in the femoral area [166]. This fat reserve is thought to serve as a store to be mobilised in feeding the new-born by lactation [167]. However, breast feeding does not seem to promote weight loss in well-nourished women [168, 169]. Quandt reported

that the number of women increasing in body fatness during lactation exceeded those experiencing fat loss [169]. Thus excessive gestational weight gain and the inability to lose this weight in the postpartum period are thought to be two of the main pathways in which reproduction contributes to overweight [144]. Excess gestational weight gain has constantly been shown to increase postpartum weight retention in the short term and has also been associated with increased weight gain in the long term [144, 165, 170]. The persistence of the post gestational weight gain as demonstrated in several cross-sectional and longitudinal studies examining women during and after childbearing demonstrated that, on average, weight is at best partially lost in lactation. However, one study revealed that although breastfeeding may not have an immediate short term weight loss benefit for the mother, at long term follow up, women who breast-fed their child for at least 3 months had a significantly lower weight gain over an average of 8.5 years [165]. In another study attempting to estimate how much of the weight change after pregnancy could be attributed to parity and breast feeding, it was concluded that lactation has a negligible role in the reduction of obesity particularly among multiparous overweight women. Weight change associated to reproduction was highly dependent on BMI previous to pregnancy. The situation gets worse among overweight women with multiple pregnancies that feature short interconceptional lengths [164]. However, Bastian et al, found that cumulative months of breastfeeding attenuated the parity effect on obesity (a positive relationship between cumulative months of breastfeeding and rates of obesity) among older women [171].

During menopause, another change in hormonal balance takes place. Menopause commences later in women with more adipose tissue [172]. But menopause per se may influence changes in body composition [6]. The increase in body weight in women approaching menopause is interrupted after menopause [173]. This pattern of change in body mass and regional fat distribution during menopause may be influenced by oestrogen medication around menopause [6].

Several mechanisms have been proposed to explain the association between number of children and obesity among women, such as insulin resistance associated with pregnancy [110, 139], hormonal alterations secondary to fewer ovulatory cycles [174-176], increased gloco-corticoid activity and the excess deposit of fat tissue that accumulates preferentially in the femoral area during pregnancy [134-136]. Many of these physiological changes associated with pregnancy have been shown to persist years after childbearing (14). In addition, motherhood and parenthood may also be associated

with changes in diet and physical activity to accommodate living with small children [143, 152]. Parents with many children may have gained weight as a result of increased food intake and changes in physical activity due to being busy and overwhelmed with rising up children.

All authors agree in the studies reviewed that among older women there is a modest relation between parity and BMI independent of age. BMI is a measure of overall body fat and is defined as weight kg/height m^2. Body mass index increases with age. Age and parity effects on body weight are highly correlated, but both effects exist independently [177], Table 5-5. In one study though, Brown et al, concluded that age had a much larger effect than parity on weight gain, and that parity was only associated with an increase in body weight of 0.55 kg per live birth after adjusting for age, education, marital status and smoking status [158]. In most of the studies reviewed, mean weight gain per child for women with one or more children range from 1.4-5.0 kg above age related increases [104, 135, 153, 162], and independent of the pre-pregnancy weight or BMI [170].

Several authors found an association between higher rates of obesity with increasing number of children among older women that was independent of socioeconomic status and other confounders. A cross sectional study from Finland found that the number of children among women aged 25-84 was closely related to the prevalence of obesity independent of marital status, occupation and smoking habits [153]. The strongest relationship between number of children and BMI was in the youngest age group (25-34), although the relationship persisted even among women aged 75-84. In another study from Sweden, the number of children was also associated with obesity among 5464 women aged 45-73 years [178]. In the USA nurses Health Study, an increase in BMI was found with increasing number of children among women aged 42-67 [158]. Among 41,000 Iowa women, mean BMI increased linearly with the number of children after adjustment for age, education, marital status and smoking [158]. Palmer et al, in a case control study found that women aged 45-69 years, with 5 or more births were more frequently obese compared with women with no births [117]. Moreover, Ness et al, found among US women aged 45-74 years who participated in the first NHANES follow-up study as well as among women aged 35-68 years who participated in the Framingham Heart Study, a significant increase in BMI with an increase in number of children [110]. The Rancho Bernardo study found as association with number of children and obesity among women many years after childbearing [179, 180]. The mean

age adjusted BMI was positively associated with number of biological children in this cohort study of women and men aged 55-84 [179]. Among men aged 50-89 years, those with 5 or more biological children were significantly more obese than men with no biological children, as estimated by BMI and W/H ratio [179].

Furthermore, Lawlor et al found a positive linear relationship between number of children and body mass index (BMI) and waist to hip ratio among both women and men [8]. The association remained significant before and after adjustment for potential confounders among women, while for men the association with BMI was weaker than women and with the W/H ratio, the association attenuated to the null after adjustment for confounders and became not significant. It was concluded that life style risk factors associated with child-rearing lead to obesity and result in increased CHD in women and men, yet biological responses of pregnancy may have additional adverse effects in women [8]. They reported that age adjusted BMI increased by 0.36 kg/m^2 per each additional child in British women, while Lao et al reported that age adjusted BMI among Chinese women increased by 0.24 kg/m^2 per child increase [181]. Hardy et al, reported that mean BMI (95% CI) increased with increasing numbers of children (P=0.01) in British women from 27.4 kg/m^2 (26.6-28.2) in those with one child to 28.6 kg/m^2 (27.6-29.6) in those with four or more children [131]. Similarly, each live birth in the Chinese women was associated with 0.45 kg, which was similar to the US women study by Brown et al, who gained 0.55 kg per live birth [158]. These variations of increase in BMI and overall obesity with the increased number of children might reflect ethnic differences among women.

Bastian et al, using data from the Cache County Study on Memory, Health, and Aging, demonstrated a dose response effect of increasing number of children on obesity after adjusting for socio-economic status, reproductive factors and important health behaviours among older women aged 66-102 years [171]. Weng et al, found a 7% increase in risk of obesity for each additional child adjusting for age, race, household income, work status, physical activity, tobacco use, and alcohol use. Moreover, they found 4% increase in risk of obesity for each additional child among men adjusting for the same covariates and the sex differences were not significantly different, which suggests physiological and behavioural mechanisms of obesity among married couples [143]. Furthermore, some investigators have proposed socioeconomic status as a significant confounder in the number of children and obesity relationship [182]. Women of less education or of lower socioeconomic class are at higher risk for obesity [183],

and that this effect may be related to personal habits such as excessive caloric intake as well as the number of children.

Less is known about changes in measures of central and abdominal adiposity associated with childbearing among women of childbearing age. A positive correlation of W/H ratio with parity has been reported in large cross sectional studies [184]. In a prospective study by Smith et al, they reported increases in W/H ratio among women who gave birth during follow up compared to those who did not [185]. The same authors in another study found that increases in waist girth were cumulative with both first and higher order births among overweight as well as normal weight women [184].

Post partum weight retention has been identified as a contributor, and studies indicate that these associated increases in WHR and WC tend to be cumulative with each pregnancy [135]. The accumulation of central adiposity, particularly that which is deposited intra-abdominally, has proven to be metabolically active and to carry more significant health risks than fat accumulation in other parts of the body [137]. WC is used as a surrogate marker for adipose tissue because it correlates well with Intra-abdominal Adipose Tissue (IAAT). Although circumference measures provide some insight into where fat is deposited with regard to girth and are considered in epidemiological studies as good measures of body fat, yet they cannot tell whether the deposition is subcutaneous or intra-abdominal [137]. So Sohlstrom et al used magnetic resonance imaging (MRI) to quantify centrally located fat and identify it as either subcutaneous or non-subcutaneous (intra abdominal adipose tissue) fat volume [186]. Their results suggested that IAAT may increase following pregnancy, potentially increasing metabolic disease risk [186]. Blaudeau et al, suggested that IAAT increases with increasing parity among women aged 18-76 years, even after adjusting for potential confounders age, percentage of body fat, physical activity and smoking [137]. This IAAT is the body fat depot most strongly related to the metabolic abnormalities of obesity [154, 187].

As stated previously, parity has also been associated with an increase in abdominal body fat distribution among older women (Table 5-5) measured by WHR. All authors agreed that the association is independent of age and BMI (table 4). The positive association of abdominal body fat distribution (high waist to hip ratio) with parity is most pronounced in pre- and peri-menopausal women, after adjustment for age and degree of obesity [6, 161], whereas post-menopausal women become more similar in their WHR [161].

In some studies examining the association between abdominal body fat distribution (WHR) and parity results were adjusted for BMI [134, 135, 161]. Ness et al reported that it is possible that the association between waist to hip ratio and parity in older women reflects an increase in overall, rather than site-specific adiposity, despite adjustments for BMI, as body mass index is a measure of body size and not of adiposity and so may not fully control for adiposity [7]. In turn, abdominal body fat distribution is related to an atherogenic lipid profile [150], hypertension [151], diabetes [158], and elevation in coronary heart disease [104].

The studies reviewed in Table 5-5, have adjusted for age and socio-economic variables. There could be other confounders and mediators that could have affected the association between greater parity and weight gain such as diet and food availability, lack of physical activity, stress levels, or parity associated changes in weight could be influenced by breastfeeding, inter-pregnancy interval, and body weight prior to each pregnancy [158]. Measures of physical activity were used in some studies. Hardy et al, found that WHR and Type II diabetes in women exhibited a linear increasing trend with increasing number of children, but these associations were largely explained by adjustment for behavioural and life style variables [131]. In this study, Hardy et al had to group women with four or more pregnancies into a single group because of lack of women with five or more children and they concluded that may be biological effects of pregnancy could be seen in women with a large number of pregnancies [131].

We can conclude from the above that social, behavioural, cultural, and biological factors are integrated in the aetiology of obesity for both women and men, but women may have additional risk due to their childbearing. Gestational weight gain and post partum weight retention (measured as increase in body weight and/or BMI and/or WC and /or W/H ratio) have a positive association with parity that may persist into later life. Among older women, BMI, WC and W/H ratio increase with increasing parity independent of age. Lifestyle factors associated with child rearing lead to obesity among women and men. Higher rates of obesity were associated with increasing number of children independent of socio-economic status and other covariates. These studies have shown that reproduction is a contributor to overweight and obesity in women of childbearing age and beyond reproductive age. Parity was positively associated with obesity. Most of the studies that have looked at the association between parity and obesity were performed either in Europe or the USA. The main mechanism by which reproduction is thought to contribute to obesity in women is through cumulative cycles of pregnancy,

weight gain and post partum weight retention in the short and long term which persists later after reproduction has ceased.

Table 5-5: Selected Studies of Parity/Gravidity,* Body Size and Body Fat Distribution among Young and Older Women

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Weng Haoling H, Bastian Lori A., et al. The Health and retirement study 2004 USA [143]	A cross sectional study of 9046 women and 4523 men examining the association between number of children and obesity in middle-aged women and men, aged 40-70 years. The sample was recruited from the cohort of the Health and retirement study.	Reported current heights and weights. BMI† was calculated and the WHO criteria of BMI ≥ 30 was used to define obesity. Reported number of children and other covariates	Obesity increased significantly with number of children among women and men. For women OR= 1.07 per child, 95% CI, 1.04-1.10 For men OR= 1.04 per child, 95% CI, 1.01-1.08	A 7% increase in risk of obesity among women for each additional child, adjusted for age, household income, race/ethnicity, work status, physical activity, tobacco use and alcohol use. A 4% increase in risk of obesity for each additional child in men, adjusting for the same covariates. This sex difference was not significant
Bastian L., Nancy A., et al. 2004 Utah, USA [171]	A population based cohort study examining number of births, other reproductive factors and health behaviours in relation to obesity risk among 2035 older women aged 66-102 years in Utah, USA	Reported heights and weights were obtained from in-person interview and recalled number of children and other reproductive health variables were obtained by a telephone interview.	The rates of obesity were significantly higher with increasing number of children, demonstrating a dose-response relationship, $p< 0.05$ The risk of obesity (OR) increased 11% with each additional live birth. Risk of obesity (OR) increased 7% with each live birth	Both mean BMI as well as the proportion who were obese increased with increasing number of children, $p<0.05$. Adjusted for age, education, marital status, BMI at age 18, use of OC, hysterectomy status, physical activity, current use of HRT and age at menarche, When nulliparous were excluded from the analysis, and adjusting for cumulative months of breastfeeding. Higher rates of obesity were found with increasing number of children that was independent of SES and other confounders

* Parity/gravidity was measured in all these studies by questionnaire.
† BMI: Body Mass Index, is a measure of body size and it is defined as weight (kg)/height (m^2)

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Gunderson, EP, Murtaugh MA et al. 2004 "Excess gains in weight and waist circumference associated with childbearing" USA [184]	A multicentre longitudinal observational study that describes the development of risk factors for coronary heart disease in 2070 women aged 18-30 years (1053 black subjects and 1017 white subjects) over 10 years. (CARDIA)	Weight and WC* measurements were obtained using standardized protocol at baseline and examinations at years 2, 5, 7 and 10. Socio-demographic, reproductive, and behavioural attributes were assessed at baseline and follow-up examinations including number of pregnancies and births. WC was selected due to the stronger correlation with central adiposity than W/H ratio. BMI was computed and subjects defined as overweight if BMI ≥ 25 kg/m^2 and normal weight if BMI < 25 kg/m^2 Central adiposity was calculated as mean WC	Gain in weight and WC associated with pregnancy and childbearing varied by race ($P < 0.001$), baseline parity (nulliparous and parous groups) ($P<0.001$) and overweight status ($P< 0.001$). Among overweight nulliparas, excess gains in weight (black subjects: 3-5 kg, white subjects: 5-6 kg) and WC (black subjects: 3-4 cm, white subjects: 5-6 cm) were associated with "short" pregnancies and one more birth(s) during follow up compared to no pregnancies ($P<0.01$ and 0.001). Among normal weight nulliparas, excess gain in weight (about 1 kg) and WC (2-3 cm) were associated with follow-up birth(s) ($P<0.05$). Among women parous at baseline: no excess weight gains were found, but excess WC gains (2-4 cm) were associated with follow-up births.	Substantial excess weight gain is associated with both short pregnancies (one or more short pregnancies but no births) and a first birth in women overweight prior to initiation of childbearing. Excess weight gain was not associated with higher order births. Increases in waist girth were cumulative with both first and higher order births among overweight as well as normal weight women.

* WC: Waist Circumference, it is a measure of central obesity.

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Smith D, Lewis C, Caveny L. 1994 "Longitudinal changes in adiposity associated with pregnancy" USA [188]	A prospective cohort study with 5 years of follow-up, of 2788 women 53% black, aged 18-30 years were assessed at baseline and reassessed after 5 years. Nulliparous women who remained so during the 5 years follow up were compared with women who had a single pregnancy in the same period	Change in body weight and in waist to hip ratio during the 5 –year period. The analysis were adjusted for demographic variables (age and education), behavioural variables (smoking and physical activity), and baseline level of adiposity	Primiparas within both race groups gained 2-3 kg more weight during the 5 years period than did nulliparas in both adjusted and unadjusted analysis. Primiparas also had greater increase in W/H ratio that was independent of weight gain. Multi parous did not differ from nulliparas in adiposity change in either race group. At each level of parity, black women demonstrated greater adverse changes in adiposity than did white women	The data suggests that women experience modest but adverse increases in body weight and fat distribution after a first pregnancy and that these changes are persistent throughout the full period.

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Coitin DC, Rosely Sichieri, et al. 2001 Brazil [164]	A national cross sectional survey of 2338 parous women, 15-49 years of age with current BMI as outcome using a two stage probability sampling of all regions of Brazil.	Weight and height were measured in households of a national representative sample of Brazilian parous women. Recalled weight prior to first pregnancy was obtained in order to better assess the relationship between reproduction and weight gain. Parity and days of predominant breastfeeding were recalled. Other explanatory variables such socio-economic, geographic, demographic and other reproductive variables were obtained by a questionnaire.	The prevalence of overweight and obesity were 25.2% and 9.3%. The overall mean weight gain per year after the first pregnancy was 0.90 kg for an average time since first pregnancy of eight years. BMI pre-pregnancy modified the association between current BMI and parity. Weight change attributed to parity was 0.6 kg greater for primiparous women with a pre-pregnancy BMI of 30 kg/m^2 compared with women with pre-pregnancy BMI of 25 kg/m^2. This greater weight retention among obese women was 1.21 kg for women with two children and 1.82 kg for women with three or more children. Parity reduced the effect of weight loss associated with lactation, 1.75 kg for six months of lactation among primiparous women and 0.87 kg among women with 3 or more children.	Weight change associated to reproduction was highly dependent on BMI previous to pregnancy and the effects of parity and lactation were small. Regression to the mean was not allowed for, so this result is of limited value.

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Blaudeau TE, Hunter GR, Sirikul B. 2006, USA [137]	A cross sectional survey of 170 women aged 18-76 years who were non-smokers with no CVD, diabetes, metabolic or endocrine disorders.	Height, weight and waist circumference were measured. Recalled parity and gravidity, physical activity and other behavioural and socio-demographic variables were assessed through a questionnaire. Physical activities, body composition (dual-energy X-ray absorptiometry, computed tomography) were measured.	Although the percent body fat was related to parity ($r=0.26$, $P< 0.01$), after adjusting for age, physical activity index, and smoking, the parity-percent body fat relationship was no longer significant. Multiple regression analysis for modelling intra-abdominal adipose tissue demonstrated that parity and intra-abdominal adipose tissue were significantly related after adjusting for percent body fat, physical activity index and smoking. (partial $r=0.18$, $P=0.02$, unstandardized $\beta = 5.22 \pm 2.26$, intercept= $- 37.32 \pm 24.63$).	Intra-abdominal adipose tissue increases with increasing parity, even after adjusting for potential confounders: age, percent body fat, physical activity, and smoking.

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Kim SA, Stein AD and Martorell R. 2006 Inter country [144]	Data was analyzed from 50 Demographic and Reproductive Health Surveys conducted between 1992-2003 to investigate the association between parity and overweight and how it is linked to country development among women of reproductive age 15-49 years	Measured weights and heights were obtained. Over weight defined as BMI ≥ 25 kg/m^2, was calculated from measured heights and weights. Parity proxied by number of live births was obtained.	Comparing women with at least parity 4 with parity 1. ORs for overweight was > 1.0 in 38 of 50 countries. The median OR was >1 in all regions studied and highest in North Africa/ West Asia, where all countries had OR > 1.0 Country wealth and development were both positively associated with the ORs. ORs were adjusted for age, household wealth, years of schooling, urban residence, short birth interval, duration of breastfeeding during recall period (35, 59 and 72 months).	Parity was positively associated with overweight in the large majority of the countries studied. The association was strongest in the North Africa/ West Asia region, where ORs exceeded one in all countries. The parity overweight relationship showed weak, positive, significant associations with both country wealth and the summary development score.
Kaye et al 1990 USA, Iowa women' health study [134]	A cross-sectional study examining the association between body fat distribution with a number of lifestyle and reproductive characteristics in 40980 post-menopausal women aged 55-69 years.	A mailed questionnaire items including parity and weight history. Self reported weight at ages 18, 30, 40, and 50 years, height, waist and hip circumference, WHR* and BMI	A J-shaped relationship was found between WHR and the number of live births. BMI increased significantly with the number of live births.	Adjusted for BMI and age. P< 0.01 WHR was significantly positively associated with age, cigarette smoking, history of infertility, number of livebirths, age at first livebirth and replacement oestrogen use

* WHR: Waist Hip Ratio is a measure of body fat distribution and it is defined as the ratio of waist circumference (cm)/hip circumference (cm).

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Heliovaara et al 1981 Finland [153]	A cross-sectional study of 17688 non-pregnant Finnish women who participatedin multiphase screening examinations for CHD and their risk factors. 1966-1972. Age of women was 25-84 years.	Weight, height, obesity defined by BMI of 30 kg/m^2 or more.	BMI increased with increasing parity .Age-adjusted prevalence of obesity increased with increasing parity compared to nulliparous women. $P < 0.001$.	Women with 10 or more previous childbirths were on average 2.3 kg/m^2 heavier than women with no births. Adjusted for age, geographical area, region, occupation, smoking and marital status.
Forster et al 1986 USA [157]	A cross-sectional study of the relationship between obesity and childbearing in white and black women (W=844, B=289) in a US population in 1978-1979.	Weight, height, BMI, and skinfold thickness.	BMI increased in black and white women with increasing parity, but was only significant in white women, $P<0.001$ Lack of significance in black women maybe due to lower sample size.	Adjusted for age, education and family income using analysis of covariance. Age at first birth increased significantly with BMI. Nulliparous women were excluded.
Brown et al 1992 USA Iowa women's health study cohort [158]	A cross-sectional study examining the relationship of life time parity and weight between age 18 and 50 years among 41184 women aged 55-69 years Response rate was 42.7%	A self reported mailed questionnaire including parity current height and weight; recalled weight at ages 18, 30, 40 & 50 years. BMI, overweight was defined as BMI>$27kg/m^2$	Parity 3+ was associated with an increase of 0.55 kg in body weight per live birth A J-shaped relationship was found between BMI and number of live-births.	Adjusted for educational level, marital status and smoking status. At each age, women with life time parity of 1 or 2 live births had lower mean body weight and BMI, and a lower proportion overweight (BMI>$27kg/m^2$), than either nulli-parous women or those with 3+ life time births.
den Tonkelaar et al 1990 The Netherlands [136]	A cross-sectional study of 11825 Dutch women who participated in the DOM project in 1984-86. Age of women 40-73	Weight, height, BMI, waist and hip circumference	In pre- and postmenopausal women a positive linear relationship was found between parity and waist hip ratio (WHR) BMI also increased with increasing parity	Adjusted for age and BMI. The relationship between parity and WHR was most pronounced in those with BMI between 20 and 25 kg/m^2 (non-obese women). Adjusted for age.

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Noppa and Bengtsson 1980, Sweden [189]	A cross-sectional study of the relationship between obesity and socio-economic factors Among 1462 middle-aged women in five age strata (38, 46, 50, 54 &60) in Gutenberg, Sweden in 1968-69.	Weight, height, body weight index (BWI) was calculated as [body wt(kg)/body ht(cm)-100] X 100	A significant positive correlation was found between number of children and body weight index, P<0.01	Adjusted for age, social class, age of husband, educational level, and husband's income.
Newcomer 1982 UK [177]	A cross-sectional study of the relationship between obesity, age, and parity in 35556 non-pregnant women attending maternal & child health clinics in 1965-79 Age of women 20-44	Weight, height, maternal weight was recorded at 20 weeks gestation and a deduction of 4 kg was made to estimate normal pre-pregnancy weight. Parity was defined as up to 4 children. Higher parity was excluded	Rate of increase in weight, increased with increasing parity.	Adjusted for height and age. Maternal weight was related to age and parity independently and that these two effects were heavily confounded.
Rodin et al 1990 Norway [135]	A cross-sectional study examining the effect of weight gain and loss due to dieting on fat distribution in randomly selected 87 non-pregnant women. Age of women 21-40 years.	Weight, height, waist and hip circumference, WHR, BMI, weight cycling index was measured by weight variability questionnaire.	WHR increased significantly with the number of pregnancies P<0.01	Adjusted for BMI and age. WHR was significantly higher for those women who were either primiparous or multiparous (parity ≥1) than for those women who were nulliparous, P<0.01.
Rissanen et al 1991 Finland [162]	A cohort study of determinants of weight gain and overweight in 6165 adult Finns who were followed up for 4-7 years. Age of women 25-64 years Baseline survey 1966-1972 Second survey 1973-1976	Weight, standing height, BMI, mean weight change and number of pregnancies between two surveys.	Weight increased significantly.with increasing parity. The relative risk of weight gain ≥ 5 kg per five years for women who initially were aged 25-44 years and had 2 or more deliveries between the surveys was twice that of women with no births during this interval. (RR = 2.0, 95% CI, 1.2-3.3)	Adjusted for education, marital status, smoking, alcohol and coffee consumption, health status, and physical activity.

Study	Design and sample size	Body size and adiposity measurements, data collected	Changes occurring with increased parity	comments
Bjorkelund et al 1996 Sweden [6]	A cohort study of 1462 women representing five separate age cohorts (38, 46, 50, 54, and 60 at the 1968-1969 baseline examination) have been followed longitudinally	Weight(kg), height(cm), waist and hip circumference(cm), waist to hip ratio(WHR),sub-cutaneous adipose tissue sample, body mass index (BMI)	Parity was positively associated with BMI, waist and hip circum-ference and abdominal obesity (WHR), P < 0.001 BMI and waist circumference increased in pre-menopausal compared to postmenopausal women	Adjusted for age. Women tend to have a significant increase in BMI and WHR when going from the pre to the postmenopausal stage, and less increase is seen after menopause. P<0.001

5.7.2 Gravidity/Parity, Cholesterol and Lipoproteins

Another possible mechanism by which pregnancy could be related to the subsequent development of coronary heart disease is through the alteration of lipid levels [140, 190, 191]. Marked increases in lipoprotein concentrations occur during pregnancy [192]. Total and low density lipoprotein cholesterol (LDL-C) and triglyceride levels progressively increase during gestation and especially during the third trimester of pregnancy [190, 193-195]. Although triglycerides have been reported to decrease rapidly during the postpartum period, total and LDL-C levels may require several months to return to baseline [190, 194]. High density lipoprotein cholesterol (HDL-C), which has been shown to be inversely associated with coronary heart disease risk in women and may be considered as the best predictor of cardiovascular risk in women among all the lipids and lipoproteins [140, 196-198], peaks at mid-gestation and then falls to levels below that found prior to pregnancy [192, 193]. This decline continues until approximately one year postpartum [7]. Gunderson et al 2004, in the largest prospective study examining the long term changes in plasma lipids associated with childbearing found that HDL-C declines associated with a first birth persist over several years, while higher order births were not associated with greater declines in HDL-C [142]. A study performed in Thailand [199] found that maternal HDL-C and TG at delivery didn't attain statistical significance with increasing parity, while total cholesterol and LDL-C increased with increasing parity.

Few studies are available on the long-term effects of pregnancy on lipoproteins; however two cross-sectional studies and three prospective studies have examined the associations among gravidity/parity, cholesterol and lipoproteins at times other than pregnancy (Table 5-6). Although there has been disagreement regarding the relationships of gravidity/parity, total cholesterol, LDL-C and triglycerides, all studies agreed that multigravid/multiparous women have lower HDL-C levels than nulligravid/nulliparous women. The magnitude of the effect between gravidity/parity and HDL-C across studies has been shown to be of the order 1 mg/dl decrease with each pregnancy or birth after controlling for potentially confounding factors such as age, smoking, alcohol use, physical activity, oral contraceptive use, education and marital status.

There has been some disagreement about the form of this association. Ness et [7], study not shown in table, and Hubert et al [200] reported a linear effect of gravidity/parity on

HDL-C levels, whereas Kritz-Silverstein et al [140], reported that for women with five or more pregnancies, HDL-C was 4.9 mg/dl (0.13mmol/L) lower than that for women with four or fewer pregnancies, whereas pregnancy was unrelated to HDL-C in women with four or fewer pregnancies. Kritz-Silverstein et al was the first to study and report the association between parity and lipoprotein among women at a time distant from their pregnancies.

Three more recent studies have reported on parity and CHD risk and risk factors. These studies are presented in Table 5-2. Lawlor et al [8] found that in women with at least two children, the number of children was associated with lower high-density lipoprotein cholesterol and higher triglyceride levels, and each additional child decreases the age-adjusted mean HDL-C by 0.02mmol/L, 95% CI (-0.03 to -0.01, p=0.001), and increases the age-adjusted mean Triglycerides by 0.02mmol/L, 95% CI (0.01 to 0.03, p=0.001). In the Rotterdam study, Humphries et al [130], described a significant trend towards lower HDL-C levels and higher total/HDL-C ratio with increasing parity, $p<0.001$. The study also found that additional adjustment for BMI, smoking and socioeconomic status did not alter this association. This study was consistent with other studies by Lewis et al [141] and Van Stiphout et al [193] where they identified significantly lower HDL-C levels in parous women than nulliparous women at 1 and 2 years after childbirth. Wollf et al [129] in the SHIP study found that women with 1 or 2 children had somewhat lower LDL-C levels whereas their HDL-C levels were minimally higher compared to parity ≥ 4. Studies of gravidity/parity and serum lipids are presented in Table 5-6.

Table 5-6: Studies of Gravidity/Parity and Serum Lipids

Study	Design	No of subjects	Exposure	Outcome	Association with high parity/gravidity	Comments
Kritz-Silverstein et al 1992 USA Rancho Bernardo [140]	A cross-sectional study of the relationship between multiparity and lipoprotein levels in women in 1984-87. Age of women 50-89	1275	Gravidity 5+ vs. 0-4	HDL-C* LDL-C† Total cholesterol Triglycerides	Low levels of HDL-C Equal levels of LDL-C Equal levels of total Cholesterol Equal levels of triglycerides	Women with gravidity 5+ had HDL-C levels that were 4.9 mg/dl lower than women with gravidity ≤ 4 ($F=7.52$, $P < 0.01$)
Flegal et al 1990 USA NHANES II [201]	A cross-sectional study of parity and HDL-C levels in white women 1976-1980. Age of women 20-50, 40-74 years.	1781 pre- 2374 post-	Pre-menopausal nulliparous parity 1-3 parity 4+ Postmenopausal nulliparous parity 1-3 parity 4+	HDL-C level	mean HDL-C levels 55.0 mg/dl 51.4 mg/dl 51.2 mg/dl 56.7 mg/dl 55.1 mg/dl 52.1 mg/dl	A significant negative association between parity and HDL-C after controlling for age, menopausal status, alcohol consumption, BMI, cigarette use, triceps and subscapular skinfold measurements, educational level, income and oral contraceptive use in both groups.
Haertel et al 1992 Germany MONICA [200, 202]	A cohort study of the associations between HDL-C and women's employment in women followed up for 3 years 1984-85 to 1987-88 Age at base-line 24-64	1998 women, employed women 905 Homemakers 985	No of previous pregnancies of employed vs. homemakers mean number of pregnancies 1.8 vs. 2.2	HDL-C	HDL-C difference between employed and homemakers women decreased from 3.4 mg/dl to 2.1 mg/dl with increasing No of children	Adjusted for age, education, marital status, BMI, coffee and alcohol consumption, cigarette smoking, physical activity and use of sex hormones. Childbearing explained only 10% of the HDL-C decrease in women who became full time homemakers.

* HDL-C, High Density Lipoprotein Cholesterol
† LDL-C, Low Density Lipoprotein Cholesterol

Study	Design	No of subjects	Exposure	Outcome	Association with high parity/gravidity	Comments
Hubert et al 1987 USA Framingham offspring study [200]	A cohort study of life-style correlates of CHD risk factor change in young adults Follow-up period 8 years, 1971-75&79-83 Age of women at entry of study 20-29 years.	497	Number of births	Total cholesterol HDL-C	A significant negative association of HDL-C and total cholesterol with increased No. of births.	Adjusted for age, education BMI, physical activity, alcohol and cigarette use, marital status, oral contraceptives use.
Lewis et al 1996 USA CARDIA study [141]	A cohort study examining the relation of parity with plasma lipids in young women at baseline, 2 and 5 years later in an ongoing study 1985-86. Age of women 18-30	2393	Nulliparous* Primiparous =1 Multiparous >1 Parous ≥ 1	HDL-C LDL-C Triglycerides	The decrease in HDL-C over the period of follow up in primiparous was significantly greater than that of nulliparous and was of similar magnitude to the results presented using all women regardless of follow up time. There was no difference for change in LDL-C or triglycerides with parity.	
Van Stiphout WAHJ et al 1987 the Netherlands [193]	A nested case-control study of the relation between pregnancy and serum lipids in 1975-1985. Average follow-up 6 years. Age of women 18-28	cases 62 control 186	1-pregnant vs. non-pregnant 2-before, during and after pregnancy 3-ever vs. never pregnant	Total cholesterol HDL-C	1-TC and HDL-C increased significantly in the 2nd and 3rd trimesters. 2-before during ↑ TC, ↑ HDL-C after ↓ TC, ↓ HDL-C 3-ever vs. never TC =, ↓HDL-C	Adjusted for age and body weight.

* Nulliparous, women who had never been pregnant; primiparous, women who were nulliparous at baseline and who had one pregnancy of ≥ 28 weeks duration between baseline and year 2; multiparous, women who were parous at baseline and who had one pregnancy of ≥ 28 weeks duration between baseline and year 2; parous, women who were parous at baseline and who had no further pregnancies during follow-up. The same apply at year 2-5

5.7.3 Gravidity/Parity, Glucose Intolerance, and Diabetes Mellitus

Pregnancy is associated with increased resistance of peripheral tissues to insulin and increased insulin secretion [203-207]. These effects may lead to worsening of glycemic control in persons with established diabetes and to gestational diabetes in the susceptible individual when maternal insulinogenic capacity is exceeded [208]. Although it is well established that obese women or women of normal weight who have had gestational diabetes are at increased risk of having type 2 diabetes in later life [207], it is still unclear whether repeated pregnancies predispose to hyperglycaemia in women without gestational diabetes [7].

Studies examining the association between gravidity/parity and subsequent incidence of non-insulin-dependant diabetes mellitus (type II diabetes) among women have been conducted since the early 50s and 60s. Some (such as Pyke) showed positive association [209], whereas others showed none [210]. However, more recent studies (Table 5-7) showed no association between gravidity/parity and NIDDM (type II diabetes) after adjusting for age and obesity [211, 212], family history of diabetes [213], as well as education and income [214]. The exception was a study by Kritz-Silverstein, where a cohort of women of relatively high socio-economic status over age 40 years showed a positive association between gravidity/parity and abnormal glucose tolerance (defined as impaired glucose tolerance and NIDDM), after adjusting for the effects of age and obesity [139]. The increased prevalence of NIDDM was confined to a small number of women with a parity of more than five. The prevalence of impaired glucose tolerance actually decreased in this group, possibly because many of these women were already defined as having NIDDM [7, 214]. The study was unable to answer the question of whether the association between parity and diabetes is linear or whether it increases exponentially after a number of pregnancies [139]. If as suggested by this study, parity 5+ is diabetogenic, it might be important to study this association. On the other hand, Simmons found a J-shaped relationship between type II diabetes and parity among Asian and European women living in the UK, where the prevalence of type II diabetes was highest among nulliparous and parity ≥ 5 among both ethnic groups compared to women who had 1 or 2 children adjusted for age and BMI [215].

Most studies have not considered the role of potential confounders such as age, obesity, history of diabetes and socio-economic status. These potential confounders have proved to play a very important role in the magnitude of the association between gravidity/parity and NIDDM in the more recent studies (Table 5-7), despite a temporary diabetogenic effect of pregnancy [211]. And there is still more controversy and debate, as Hanely et al found no association between the number of births and risk of type II diabetes when parity was analyzed as a continuous variable [204]. Cheung, however, from Australia found a significant association between parity and age at diagnosis of diabetes for women with type II diabetes mellitus, but when further adjustments were made in the same study for year of birth, BMI and positive family history, the effect in the overall cohort disappeared, but it persisted when subjects with parity > 5 were compared with nulliparous [216]. In another study conducted in Qatar, the authors found parity to be a risk factor for type II diabetes and that type II diabetes increased with increasing parity adjusting for age and gender [217]. Nicholson et al, found in a study among Caucasian and African American women that parity incidence rates were highest among women with five or more live births and lowest among women with one to two live births, adjusting for socio-demographic factors and higher obesity. And after adjustment for all covariates (socio-demographic, clinical, lifestyle factors and inflammatory markers), grand-multiparity ≥ 5 was still associated with a 27% increased risk for diabetes (hazard ratio 1.27, 95% CI (1.02-1.57) [203].

On the whole, the studies reviewed showed little or no association between parity and the development of type II diabetes after controlling for the effects of confounders. This suggests that the association between gravidity/parity and diabetes might be confounded or mediated by other factors such as age, obesity and socio-economic status. On the other hand, many studies had shown the association remained significant at parity ≥ 5.

High parity is unlikely to have an important impact on development of chronic diseases in the USA and other industrialised countries, where few women have more than six children. Exposure to high parity may be very relevant however for a number of developing countries where many more women bear 6 or more children. Studies of parity and chronic disease risk have not been done in many developing countries. Therefore in this study, the association between parity and risk of type II diabetes have been investigated where women bear many children and chronic diseases are on the rise.

Table 5-7: Gravidity/Parity, Glucose Intolerance and Diabetes Mellitus

Study	Design	No of subjects	Exposure	Outcome	Adjusted RR*	95% CI†	Comments
Manson et al 1992 USA The Nurses' Health Study [211]	A cohort study examining the association between parity and incidence of NIDDM‡ among nurses. Follow-up period 12 (years), 1976-1988. Age of nurses 30-50 years	113606	Parity 6+ vs. nulliparous	Incidence of confirmed NIDDM	1.56 0.95	1.27-1.91 0.75-1.19	An apparent association between parity and diabetes was observed in unadjusted analyses (RR=1.56. 95% CI, 1.27-1.91) among women with 6+ births compared to nulli-parous women, but was abolished after adjustment for age as a confounder and BMI as a mediator. Adjusted for age and body mass index (BMI).
Kritz-Silverstein et al 1989 USA The Rancho Bernardo study [139]	A cohort study examining the independent relation of parity to NIDDM and IGT§ in women. 1984-87. Age of women ≥ 40 years.	1186	Parity vs. nulliparity mean live-births 1.7	IGT NIDDM	1.10 1.16	1.01-1.19 1.04-1.29	Adjusted for age, obesity, and family history. The slight increase in the risk of IGT and NIDDM with increasing parity many years after childbearing could not be explained by obesity, although obesity was significantly associated with an increased risk of both NIDDM and IGT.
Collins et al 1991 Australia [213]	A cross-sectional study examining evidence against association between parity and NIDDM and IGT in four pacific, and Indian Ocean island nations. Age of women ≥ 40 years.	2736	parity vs. nulliparity	NIDDM IGT	OR** <1 OR <1	- -	Adjusted for age, BMI and family history of diabetes. An inconsistent relationship between No of full term pregnancies and the prevalence of IGT and NIDDM, although in each population, there was a higher prevalence of NIDDM in the highest parity group ≥10 compared with the lowest parity group 1-3.

* RR, Relative Risk
† CI, Confidence Interval
‡ NIDDM, Non-Insulin-Dependent Diabetes Mellitus
§ IGT, Impaired Glucose Tolerance
** OR, Odds Ratio.

Study	Design	No of subjects	Exposure	Outcome	Adjusted RR*	95% CI†	Comments
Boyko et al 1990 USA NHANES [214]	A cross-sectional study examining the effects of childbearing on subsequent glucose tolerance and NIDDM prevalence among women	3057	parity 1 vs. parity 0	NIDDM Plasma glucose fasting & 2-hours	1.07	0.98-1.17	Adjusted for age, BMI, education and income. Before adjustments, there was a significant linear increase in diabetes prevalence and either plasma glucose measurements with increasing No of livebirths. Unadjusted RR for NIDDM 1.73, 95% CI 1.39-2.15.
Pyke DA 1956 UK [209]	A cross-sectional study looking at parity and prevalence of diabetes among women.	583	Parity 5+ vs. nulliparous	Diabetes Mellitus	-	-	Women who has had five or more children appear to have about 3 times as great a chance of developing diabetes as a woman who has had none.
Alderman et al 1993 Australia [212]	A case-control study examining reproductive history, glucose tolerance and NIDDM in Hispanic and non-Hispanic women. Age of women 20-74 years	Cases 196 Controls 735	Parity vs. nulliparity	NIDDM IGT	OR=1.04 Per birth P=0.18		Adjusted for sub-scapular skin-fold thickness. The relative odds of NIDDM for the live-birth number, which was small and borderline significance, diminished after adjustment. Similar findings were observed for IGT.

Study	Design	No of subjects	Exposure	Outcome	Adjusted RR*	95% CI†	Comments
Simmons D 1992 UK [215]	A cross sectional survey examining the prevalence of type II diabetes in relation to parity in two groups of South Asian and European women living in the UK	2096 European (68 with diagnosed diabetes) and 1148 Asian women (95 with diagnosed diabetes)	Parity Nulliparous Parity ≥ 5	Prevalence of type II diabetes	Prevalence Europeans 4.4% Asians 16.3% European 6.3% Asians 16.5%		In those aged 30-64 years, the age and BMI adjusted prevalence of type II diabetes was highest among nulliparous and grand-multiparous Among both Europeans and Asians women, those with 1 or 2 deliveries had diabetes less frequently than either nulliparous or those with parity 5 or more (P <0.001 in both ethnic groups). Parity had no effect among women aged ≥ 65 years.
Cheung N.W. 2004 Australia [216]	A retrospective analysis of data extracted from a diabetes service database on 2102 women with type II diabetes		Parity	Age at diagnosis of diabetes	β* = -0.25	S.E. ± 0.08, P= 0.002	Adjusting for year of birth. There was a significant association between parity and age at diagnosis of diabetes, when age of diagnosis was regressed on parity. For an increase of parity one, the age of diagnosis decreased by 0.25 years. When further adjustments were made for year of birth, BMI and positive family history, the effect on the overall cohort disappeared, but it persisted in subjects born before 1950 (β = -0.17 ± 0.1, p= 0.09), or with parity > 5 (β = - 0.60 ± 0.25, p= 0.02)

*β: regression coefficient

Study	Design	No of subjects	Exposure	Outcome	Adjusted RR*	95% CI†	Comments
Hanley, A et al 2002 Canada [204]	A population based cross sectional survey to determine the prevalence of type II diabetes and its associated risk factors. Analysis was performed on 383 women aged 12-79 years who provided fasting blood samples for glucose, insulin and proinsulin		Parity Nulliparous vs. ≥ 1 birth	Type II diabetes	OR 0.43	0.19-0.94, p<0.05	Women who had at least one live birth had a significantly reduced risk of type II diabetes after adjustment for age, waist circumference and oral contraceptives. When analyzed as a continuous variable, the number of births did not appear to be associated with risk of diabetes (OR 0.94, 95% CI 0.83-1.06, p=0.28).
				Fasting insulin and proinsulin			Nondiabetic nulliparous women had significantly elevated concentrations of fasting insulin and proinsulin relative to nondiabetic parous women, adjusting for age, waist circumference and oral contraceptive use
Nicholson WK et al 2006 USA [203]	A population-based prospective cohort study of 7024 Caucasian and African-American women from the Atherosclerosis Risk in communities study, a prospective epidemiological study of men and women aged 45-64 years, with 9 years of follow up. Parity and risk of diabetes was estimated for 754 incident cases of diabetes with Cox proportional hazard regression models		Parity	Incidence rate of diabetes	23/1000 person-years for parity ≥ 5	20.3-26.7	Diabetes incidence rates were highest among women with five or more live births and lowest among women with one to two live births, adjusting for socio-demographic factors and higher obesity.
					11/1000 person-years for parity 1-2 live births	9.6-12.5	After adjustment for all covariates (socio-demographic, clinical, lifestyle factors and inflammatory markers), grandmultiparity ≥ 5 was still associated with a 27% increased risk for diabetes (hazard ratio 1.27, 95% CI 1.02-1.57)

Study	Design	No of subjects	Exposure	Outcome	Adjusted RR*	95% CI†	Comments
Bener A, Zirie M, Al-Rikabi A Qatar 2005 [217]	A case control study examining the association between consanguineous marriages, obesity, environmental risk factors associated with type II diabetes between diabetic patients and healthy subjects.	Cases 338 Controls 338	Parity	Type II diabetes	OR 1.34	1.02-1.77, p=0.037	Adjusted for age and gender, there was a statistically significant difference between diabetic and control subjects with respect to number of children. Therefore number of children was considered as a risk factor for type II diabetes.

5.7.4 Gravidity/Parity and Hypertension

The relationship between gravidity/parity and subsequent hypertension in women has been studied in various populations. The reports of these relationships have been inconsistent. Tables 5-8 and 5-9 present a summary of these results.

Of these 19 studies, conducted since 1945, nine found no association between gravidity/parity and blood pressure [8, 130, 218-224]. The remaining ten studies fall in 3 patterns: an inverse association between gravidity/parity and blood pressure [225-229]; blood pressure tending to be lowest in women with two to five children and rising in women with six or more children [230, 231]; or blood pressure tending to be higher with less than 2 children and more than two children [129]; or a protective effect of gravidity/parity that interact with age to give an inverse association for younger subgroups of women [223, 224, 232, 233], and none for older women. Few studies have adjusted for the effects of age, obesity, cigarette smoking, alcohol consumption, socio-economic status, exercise and oestrogen use, which may affect blood pressure and be correlated with parity.

The physiological mechanisms for a negative association between number of pregnancies and blood pressure are unknown. A speculative possibility is that it may be related to the repeated adaptation of the vascular system to the increase in plasma volume that occurs during pregnancy [232]. Therefore, a better understanding of this relationship might help to elucidate both the mechanisms of blood pressure control and the long term effects of repeated pregnancies on women's health [232].

Table 5-8: Studies of Gravidity/Parity and Hypertension

Author & Study	Year published	Study Group	Findings for Systolic (SBP) and Diastolic (DPB) Blood Pressure
Ness et al NHANES II [232]	1993	A cross-sectional study of 4626 white women (1841 premenopausal & 2785 postmenopausal), aged 20-70 years, who were examined in the Second National Health & Nutrition Examination Survey for the association of number of pregnancies to blood pressure and hypertension in 1976-1980	In univariate analyses: neither mean SBP, mean DPB, nor prevalence of hypertension varied systematically with the No. of pregnancies. In multivariate analyses: a slight decline of SBP with greater gravidity after adjustments for age, body size, smoking, oral contraceptive use, education, poverty status and alcohol use. The association of gravidity with SBP was stronger for younger premenopausal women. The odds of hypertension declined with each additional pregnancy compared with no pregnancies. There was an odds ratio of 0.90 (95% CI=0.81-0.99) for premenopausal women and OR of 0.95 (95% CI=0.92-0.98) for postmenopausal women.
Kritz-Silverstein et al. The Rancho Bernardo study [218]	1989	A cross-sectional cohort of 1093 upper middle class Caucasian women aged 50 years or more at the follow-up visit. Mean parity=1.8, mean gravidity=2.2. 1045 men aged 50+ were included as well. 1984-1987	No association was found between parity or gravidity and hypertension or blood pressure after controlling for a variety of covariates such as age, obesity, alcohol intake, cigarette smoking, exercise and oestrogen use. No association was found between parity and hypertension among men, which reduces a possibility of a non-biological psychological or social support phenomenon related to having children that might prevent high blood pressure
RAO et al India [220]	1984	A cross-sectional study of blood pressure measures among 961 rural and 1073 urban women aged 16-45 years in south India. 60% of women were under age 30 years.	The blood pressure levels showed a lack of specific trend with parity (0, 1, 2, 3, 4, 5+), or gravidity. Significant differences exist ($p< 0.01$) in all parities (0-5+) between rural and urban areas.
Lee-Feldstein et al USA [219]	1980	Blood pressure of 755 white and black women from Detroit Michigan were analysed in relation to parity, race, and residential area.	SBP and DBP were found to be significantly different for black and white females, higher on average for black women. No independent association between parity and systolic or diastolic blood pressure. However a negative trend between parity and systolic blood pressure for white women of low socio-economic status was reported after adjusting for age, body size, race and residential area.

Author & Study	Year published	Study Group	Findings for Systolic (SBP) and Diastolic (DPB) Blood Pressure
Humphries K, Westendorp I, et al, The Rotterdam study Netherlands [130]	2001	A population-based study comprising of 2681 postmenopausal women aged 55 – 99 years who participated in the Rotterdam study	Neither mean age-adjusted systolic and diastolic blood pressure nor the prevalence of hypertension varied with parity.
Lawlor DA, Emberson, Ebrahim Shah, JR, et al UK [8]	2003	A cross sectional study of 4286 women and 4252 men from 24 British towns. Among women: mean parity 2.3 Among men: mean parity 2.2	No linear association was found between number of children and mean age adjusted systolic blood pressure or mean age adjusted diastolic blood pressure with both men and women, even though the sample included women with more than five children. (Difference per increase of one child for SBP= 0.31 (95% CI: -0.33 to 0.94, p=0.35), for DBP = 0.05 (95% CI: -0.26 to 0.35, p=0.77).
Wolff B, Volzke H, et al Study of Health in Pomerania Germany [129]	2005	A cross sectional study of a sample of 1195 women drawn from a larger population study in West Pomerania, the Northeast Coastal Region of Germany	Compared with women with 2 children, those with < 2 and those with >2 had marginally higher mean age adjusted systolic blood pressure values, p<0.001 and accordingly found a greater proportion of subjects with hypertension.
Duda RB, Kim MP, Darko R, et al USA [230]	2006	A community based survey to determine the burden of illness in a sample of 1328 adult urban women as part of the Women's Health study of Accra, USA	Parity of three or more children was a significant risk factor for elevated blood pressure (OR= 5.16, 95% CI: 2.90-9.19, p<0.001), while nulliparity was a significant protective factor among those women
Strevens H, Wide-swensson D, Ingemarsson I Sweden [229]	2001	A cohort study of 600 women in an attempt to establish normal levels of blood pressure in the pregnant population in order to recognize pathology	Parity significantly influenced DBP at term. Multiparous have significantly lower DBP levels in pregnancy compared to nulliparous. The first pregnancy seems to have the greatest impact in lowering the blood pressure in subsequent pregnancies

Table 5-9: Summary of Earlier Study Results for Parity and Blood Pressure (BP) in Females*

Author & Study	Year published	Study Group	Findings for Systolic (SBP) and Diastolic (DPB) Blood Pressure
Barnes and Browne [221]	1945	Non-pregnant women at London hospital (915 nulliparous and 1041 parous).	Parous women: parity found to have no effect on mean blood pressure. No difference in mean BP between nulliparous and parous women found.
Humerfelt and Wedervang [225]	1957	1350 women aged 40-42 years surveyed in Bergen, Norway.	Mean BP found to be similar for married women with 0 or 1 child. Mean BP especially systolic and incidence of hypertension clearly lower in women with 2 or more children.
Miall and Oldham [226]	1958	155 Welsh women aged 15-45 years in an urban mining valley and in an agricultural area.	Family size found to be inversely correlated with BP.
Miall and Oldham [227]	1959	4-year follow-up of Welsh women in mining valley.	For several 5-year age groups, mean BP fell for women bearing a child in interval between surveys. In No. 5-year age group did women having no children in interval experience drop in mean BP.
Johnson and Remington [234]	1961	694 black women aged 20-60+ years in Nassau Bahamas.	No clear relationship between parity and BP found.
Miall et al [231]	1962	1430 black women aged 15-59 years in Jamaica.	Nulliparous women tended to have higher mean BPs than parous women. Below age 55 years, mean BPs were lowest in those with 2-5 children and rose in women with 6 or more children.
Schneckloth et al [233]	1962	Black women in three villages in St. Kitts, West Indies.	No clear trend of BP with family size reported. Among 766 women with no history of toxaemia, the 30-49 year old group showed greater proportion of nulliparous than parous with elevated diastolic BP.
Parry, EHO [223]	1969	877 Ethiopian women aged 20-69 years at TB clinic (a very small percent had sputum-positive TB).	Among women 30-49 years of age, systolic blood pressure was higher in nulliparous than parous women; no relationship of SBP to multiparity found, and no relationship of DBP to parity found.
Ree, GH [228]	1973	103 West African rural women aged 25-44 years.	Both SBP and DBP were lower in women with 3 or more children than in women with 0-2 children.
Akinkugbe, A. [224]	1976	626 non-pregnant Nigerian women aged 15-44 years.	Only in women aged 30-34 years did systolic BP decrease with increasing parity. Otherwise, no relationship between BP and parity was found.

* Taken from Lee-Feldstein et al 1980

5.8 Parity and the Metabolic Syndrome

The metabolic syndrome is described as the co-occurrence of abnormalities in glucose and lipid metabolism, abdominal fat distribution and blood pressure [235]. It is defined by a high value of a score based on waist circumference ≥ 90 cm for men or ≥ 80 cm for women, plus any two of: (a) raised triglycerides (TG) level (≥150 mg/dl) equivalent to (1.7 mmol/L) or specific treatment for this lipid abnormality; (b) reduced high density lipoprotein (HDL-C) (<40 mg/dl {1 mmol/L} in males and <50 mg/dl {1.3 mmol/L} in females) or specific treatment for this lipid abnormality; (c) raised blood pressure (BP, systolic BP ≥130 mmHg or diastolic BP ≥85 mmHg) or hypertension therapy; and (d) raised fasting glucose (≥100 mg/dl) equivalent to {5.6 mmol/L} or previously diagnosed type II diabetes. The metabolic syndrome has been linked to the development of CVD, diabetes and overall mortality [236-239].

People with abnormal glucose and lipid metabolism, obesity and abdominal fat distribution and hypertension constitute a major challenge facing health systems in developed countries. The situation is more complex in developing countries where resources are scarce and limited. These people are at substantial risk of developing diabetes and cardiovascular diseases including coronary heart disease, cerebrovascular disease and stroke that requires long term care [240].

Several studies performed among the Arab populations in the Middle East and Gulf countries, illustrated high prevalence of diabetes, impaired glucose tolerance, obesity and hypertension [241-248]. However, all of these studies have focused on estimating the population distribution of major risk factors for CVD and only two studies estimated the clustering of such risk factors in individuals in the form of the metabolic syndrome [240, 249]. Although these studies have used different definitions of the metabolic syndrome, they both found the metabolic syndrome to be more prevailing among women. Abdul-Rahim and colleagues used the WHO definition [250], while Al-Lawati et al, used the national Cholesterol Education programme - Third Adult Treatment Panel III definition to estimate the prevalence of the metabolic syndrome [235]. However, none of these studies have examined reproductive history and in particular parity as a risk factor for the development of the metabolic syndrome.

Most of the studies that have examined the association between parity and or pregnancies and each component of the metabolic syndrome were performed in Europe

and USA. Few were performed in developing countries. Only two recent studies [181, 251] have assessed the relationship between parity and the combination of these risk factors as part of the current definition of the metabolic syndrome using two different definitions. The study that was performed in China has shown that higher parity was associated with a consistent increase in the risk of the metabolic syndrome among women and men after adjustment for age, socio-demographic, reproductive and behavioural factors. When the association was adjusted for BMI, it attenuated in men but not in women suggesting that the association with metabolic syndrome in women is likely to represent a biological response to pregnancy [181]. On the other hand, the second study conducted in the USA, found that the rate of the metabolic syndrome was significantly higher with increasing numbers of children, demonstrating a dose response relationship $P<0.0001$. The odds of the metabolic syndrome increased 13% with each additional child after controlling for age, race/ethnicity, income, education, reproductive and behavioural risk factors. After adjustment for BMI, the strength of the association was decreased suggesting that weight might be an important mediator of the effect of parity on the risk of the metabolic syndrome [251]. Both studies have used different definition for the metabolic syndrome in assessing the association between parity and the metabolic syndrome. The Chinese study used the International Diabetes Federation (IDF) definition 2005 [252], while the American study used the Third Report of the National Cholesterol Education Programme Expert Panel on the Detection, Evaluation and Treatment of High Blood Pressure in Adults definition (ATP III) [235].

The International Diabetes Federation in 2005 formulated a new worldwide definition of the metabolic syndrome that addresses both clinical and research needs in different countries and across various ethnic groups. This definition was endorsed by WHO. Using different definitions for the metabolic syndrome makes comparison of results from different studies difficult.

Understanding the role parity plays in the development of the metabolic syndrome would have implications for preventing CVD, diabetes and other conditions associated with the metabolic syndrome. To our knowledge, no prior study has examined the relationship between parity and the clustering of these components as part of the current worldwide IDF definition of metabolic syndrome among Palestinian women living in refugee camps.

Table 5-10: Studies of Parity with the Metabolic Syndrome

Author(s) & year	Study design	Exposure	Outcome	RR	95% CI	Comments
Cohen Adi, Pieper, C et al USA NHANES 2006 [251]	Cross sectional data was extracted from the Third National Health and Nutrition Survey to examine the effect of parity and breastfeeding on the prevalence of metabolic syndrome as described in the ATP III among 4699 women aged ≥ 20 years	Parity	Prevalence of the metabolic syndrome	A dose response relationship	P<0.0001	The prevalence of the metabolic syndrome was significantly higher with increasing numbers of children, demonstrating a dose response relationship<0.0001
				OR 13% increase per additional child	6%-20%	The odds of the metabolic syndrome increased 13% with each additional child after controlling for age, race/ethnicity, income, education, reproductive and behavioural risk factors.
		History of breast-feeding		OR decreased 22%	1%-39%	The odds of the MS decreased 22% in women with a history of BF > 1 month adjusting for the same covariates as above. Both effects were no longer significant after adjustment for BMI
Lao, X.Q. Thomas, G.N. et al The Guangzhou Biobank Cohort Study China 2006 [181]	A cross sectional study drawn from a large cohort study examining whether parity or gravidity contributes to the development of the metabolic syndrome among 7352 women and 3065 men aged 50-93 years	Parity Gravidity	Prevalence of the metabolic syndrome	OR per birth 1.16 OR change per pregnancy 1.11	1.11-1.22 1.06-1.16	The age adjusted prevalence of the metabolic syndrome increased with number of births and pregnancies in women. The association persisted even after adjustment for lifestyle factors, socioeconomic factors and reproductive factors. With men the association attenuated after adjustment for BMI, implying that the association in women may represent a biological response to pregnancy.

5.9 Proposed Mechanisms for the Association between Gravidity/Parity and Coronary Heart Disease Risk Factors in Women

Women with many pregnancies and live births and early age at first birth have a modestly increased risk of developing CHD according to studies reviewed in Tables 5-2, 5-3, and 5-4. Specific mechanisms by which the association is mediated are not known. As a result of the uncertainty, four explanations have been proposed:

- Repeated pregnancies lead to metabolic and physiologic changes that elevate CHD risk.
- Pregnancy results in lifestyle changes and stress that cannot be measured by biologic assays but tend in turn to elevate CHD risk [7]
- Physiological effects of pregnancy and childbearing interact with stress and lifestyle factors. Hormonal alterations occurring during pregnancy in combination with stress occurring during childbearing could lead to CHD morbidity and mortality [110, 112, 114].
- Confounding factors such as socio-economic status, which could be related to both the exposure (gravidity/parity and age at first birth) and the outcome of interest (CHD morbidity and mortality) may account for the reported association. If the association is confounded by socio-economic status, then it is not the number of pregnancies per se that is causing CHD but the confounding effect [133].

5.9.1 Biological Plausibility for an Association

All observational studies examining the association between gravidity/parity and body weight gain and fat distribution have shown positive effects, suggesting that the association is real. Parity related weight gain and fat deposition may have different metabolic effects: they can raise blood pressure, increase serum total cholesterol, decrease HDL-C levels, and induce glucose intolerance [158]. Since each of these factors can increase the risk of CHD, the influence of obesity might be explained by its action on these known factors.

Another mechanism by which gravidity/parity could be related to the subsequent development of CHD is through the direct alterations of lipid levels. Marked fluctuation in lipoprotein concentration occurs during pregnancy. Studies examining the long-term effects

of pregnancy on lipoproteins showed that multigravid/multiparous women have lower HDL-C levels than nulligravid/nulliparous women. Changes in HDL-C are particularly important to any discussion of CHD risk in women, since low HDL-C is the most powerful predictor of heart disease in women [140]. Most studies that have examined the association between gravidity/parity and the development of diabetes mellitus in women have shown that the association might not be a cause-effect relation, but rather it has been mediated by other factors in particular obesity, despite a temporary diabetogenic effect of pregnancy. Only one study has shown an association but with 5+ children [140]. The same applies to the association between gravidity/parity and hypertension where most studies showed no or negative association.

Alternatively, it has been proposed that pregnancy represents one type of weight variability or weight cycling [253]. Weight variability has been shown to relate to greater upper body fat distribution [135], and higher CHD incidence [254] perhaps through the mechanism of hyperinsulimia. The atherogenic risk factors associated with gravidity/parity includes reductions in HDL-C, increases in body size, and changes in body fat distribution [7].

5.9.2 Stress and Lifestyle as Potential Explanations

Pregnancy and rearing many children may be associated with changes in behavioural factors such as eating a high fat diet, sedentary lifestyle and smoking which in turn increases the risk of CHD. Ness et al [7], proposed that caring for young children resembles a stressful occupational situation. Karasek et al, showed that when a job is very demanding, and where one can't control the job situation, such stressful environment could lead to CHD risk [255]. Ness et al [7], proposed that stress experienced during childbearing may be associated with anatomic changes in coronary arteries which do not present as clinical disease until later life, when compounded by the events of ageing.

Stress and lack of sense of control may elevate blood pressure and blood cholesterol levels, and contribute to behaviours that are considered as stress reducing, but which can increase CHD risk such as smoking, overeating and in certain cases, excessive drinking [256].

5.9.3 Confounding as a Potential Explanation

When only observational data are available, it is difficult to discount the role of unmeasured confounding factors, which may, rather than gravidity/parity and age at first birth, result in the observed effect on CHD. For example some women are compelled to have many children as a result of religious beliefs or political conflict as in the case of the Palestinian women and these factors themselves may be independently associated with CHD risk.

It has been found that socio-economic status plays a very important role in determining the magnitude of the association between gravidity/parity, age at first birth and CHD risks [117, 162, 166]. Lower social-class women tend to have an early age at first pregnancy, and age at first pregnancy is a major determinant of multiparity [94]. Thus social class could be the attribute associated with heart disease. for example, Croft and Hannaford, found that women with 5+ pregnancies had a 1.8 fold increased risk of myocardial infarction before adjusting for social class and cigarette smoking; after adjustment, the relative risk was 0.9 [123]. There have been some inconsistencies among the studies reviewed concerning adjustments for socio-economic status. Ness et al, adjusted for education and income, but the magnitude of the association between gravidity/parity and CHD risk remains the same [110].

In summary, the studies reviewed have shown that parity and gravidity have been associated with increased body weight and greater central body fat distribution as well as decreased HDL-C level and CHD. Although the magnitude of the association is often small and despite the inconsistencies in the different studies regarding the association between parity/ gravidity and CHD risk, yet this review had shed light on the proposed mechanisms or risk factors by which the association is mediated and by which CHD develops in women.

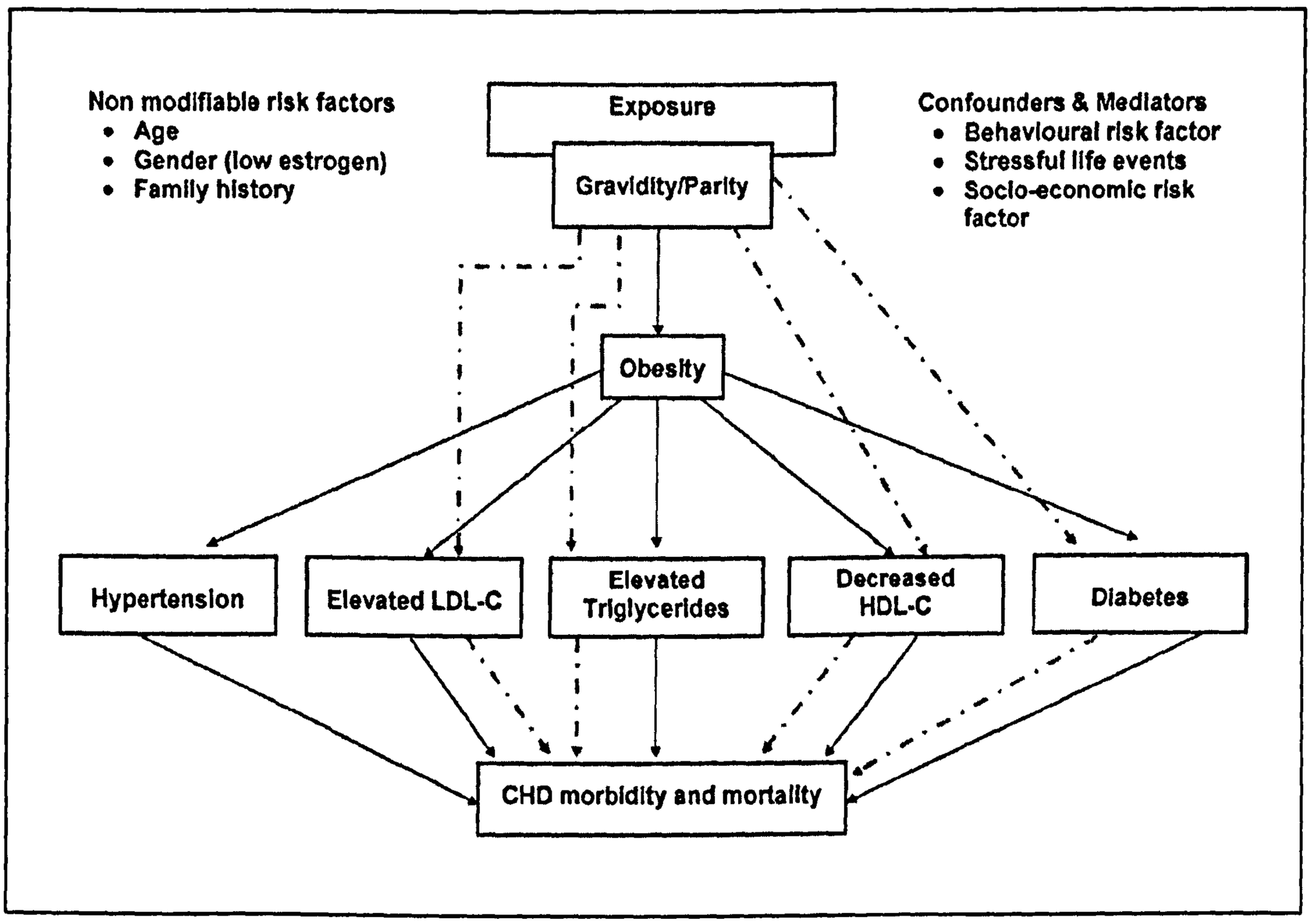
5.10 Development of the Conceptual Framework and Research Hypotheses

5.10.1 Conceptual Framework

Based on the results of the literature review of studying the association between gravidity/ parity as an exposure variable and CHD risk factors (obesity, hyperlipidemia, diabetes and hypertension) as outcome variables, the following conceptual framework (Figure 5-1) was

developed. This conceptual framework discusses the different pathways that gravidity/parity exerts its effects on CHD morbidity and mortality. It also views the association between gravidity/parity and CHD risk to be a result of a combination of demographic, biological, physiological, socio-economic, and environmental factors. This conceptual framework constitutes the basis for the analytical framework used for all the analysis in the thesis.

Figure 5-1: Conceptual Framework



As discussed in the literature review, repeated pregnancies and childbirths will lead to metabolic and physiological changes that elevate CHD. The process can go via different scenarios:

Scenario one: Gravidity/parity leads to increase in body weight and body fat distribution. Parity related weight gain and fat deposition may have different metabolic effects:

a. It raises Blood pressure

b. It increases TG, T-Cholesterol, LDL-C and decreases HDL-C

c. It induces glucose intolerance

Since all these factors can increase the risk of CHD, the influence of obesity, promoted by higher parity, might be explained by its action on these risk factors.

Scenario two: Pregnancy is a state of insulin resistance and the process of being pregnant and having children induces a lot of metabolic and physiological changes on the lipid and the carbohydrates metabolism that leads to subsequent development of CHD through

1. Alterations of the lipid profile which causes HDL-c to decrease and TG, T-Cholesterol, LDL-C to increase and which in turn will lead to CHD morbidity and mortality.
2. It also produces changes on the carbohydrates metabolism and will make women more susceptible to diabetes especially if they have a family history of diabetes. The association between gravidity/parity and the development of type II diabetes in women might not be a cause effect relation, but rather it is mediated by other factors such as obesity, despite a temporary diabetogenic effect.

Scenario three: Pregnancy and child raising may lead to a stressful environment and changes in behavioral factors such as changes in dietary patterns, sedentary lifestyle and smoking which interact with the metabolic and physiological changes of pregnancy and in turn increases the risk of CHD.

Scenario four: Socio-economic status could play an important role in the association between gravidity/parity and CHD risk. Women of lower social class will marry at a younger age and will have an early age at first pregnancy and childbirth and therefore will bear more children. They will have lower educational attainment, higher unemployment and therefore lower income, and will smoke more and therefore will be at increased CHD risk. In observational studies, there will be always a space for unmeasured confounding factors which may result in the observed effect on CHD rather than gravidity/

parity. Some women might have more children as a result of religious beliefs or political conflict.

5.10.2 Research Hypotheses

Based on the literature review presented in Chapter Five, eight hypotheses were developed relating gravidity/parity with CHD risk mortality and morbidity. These hypotheses will be tested in the results chapter. The following are the hypotheses investigated:

Hypothesis one: an increasing number of children is associated with an increasing risk of obesity among Palestinian women aged 40-65 years independent of socioeconomic status, other reproductive and lifestyle factors.

Hypothesis two: an increasing number of children is associated with increasing waist circumference and therefore increasing central obesity among Palestinian women living in refugee camps independent of socioeconomic status, other reproductive and lifestyle factors.

Hypothesis three: an increasing number of children is associated with an increasing waist to hip ratio among Palestinian women living in refugee camps independent of socioeconomic status, reproductive and lifestyle factors.

Hypothesis four: An increasing number of children is associated with an increasing risk of elevated lipids and lipoproteins among Palestinian women living in refugee camps independent of socioeconomic status, reproductive and lifestyle factors.

Hypothesis five: An increasing number of children is associated with an increasing risk of developing type 2 diabetes mellitus among Palestinian women living in refugee camps independent of socioeconomic status, reproductive and lifestyle factors.

Hypothesis six: An increasing number of children is associated with an elevation in SBP, DBP and hypertension among Palestinian women living in refugee camps independent of socioeconomic status, reproductive and lifestyle factors.

Hypothesis seven: An increasing number of children is associated with an increasing risk of developing CHD in the form of women's reports of present or past CHD events.

Hypothesis eight: An increasing number of children is associated with the development of the metabolic syndrome among women in the refugee camps.

Chapter 6
RESEARCH METHODOLOGY

6.1 Research Context

The prevailing conditions under which this research was prepared and conducted were strongly shaped by the political and economic development within the Palestinian territories as well as the psychological status of the women participating in the research.

6.1.1 Political Developments

Preparation for the field work and the actual implementation took place at a very difficult time in the history of the Palestinian people as the Second Popular Uprising (Intifada) started in September 2000. From September 2000 to 2004, a health system crisis emerged as around 4,000 Palestinians died and around 45,000 were injured; infrastructure including hospitals and clinics were destroyed and shelled by the Israeli armed forces. This situation led to very severe undermining of already fragile public institutions and services and influenced greatly the health of the people as well as the nature of the Palestinian health care system.

Another major factor contributing to the difficulty of conducting the research was the Israeli closure policy with its restrictions on movement. There have also been extensive curfews imposed on towns, villages and refugee camps for prolonged periods. The peak of these Israeli measures was reflected in the large-scale destruction, killing and restrictions during the Israeli incursion into the main towns of the West Bank and Gaza Strip from March to April 2002. The situation since the re-invasion of Palestinian-controlled areas has become even more critical.

All these factors made the mobility needed to conduct the research very difficult, even to travel to nearby cities and villages from my residence area in Ramallah city. Moreover, living near an Israeli settlement in the West Bank led to our exposure to continuous gunfire and shelling from Israeli tanks. For five consecutive months, our living room was transformed to a kitchen and bedrooms, and we used to sleep on mattresses on the floor. My bedroom was burned and my eldest son was shot twice in his shoulder and foot with rubber

bullets. My children were young and I faced many psychological problems with them due to the sound of the shelling from guns and tanks as well as the gunfire from Apache helicopters and F16's.

6.1.2 The Psychological Status of Women

In spite of this difficult situation, it was a challenge to go ahead with the fieldwork, particularly as the study area was Palestinian refugee camps that were the constant target of the Israeli army: Many families had lost their children as well as their bread winners. Nevertheless, data collection was conducted under gunfire and curfews. It was time consuming as often only two interviews or even none could be conducted within a day due to the unpredictability of the situation.

As mentioned above, many of the women participating in the study had lost one or more of their children or their husbands or relatives. However, in spite of their mourning and sadness, they agreed to participate actively in the study revealing their resilience and hope for a better future even when their lives appeared so totally reduced. For example, Huda living in Kalandia refugee camp had a husband imprisoned for 8 years and a son imprisoned for 4 years. She was left with no breadwinner in the family and the only son that could help the family survive was injured by Israeli shelling of the camp. In spite of that she still had hope for a better future. Alia from the same camp had her 14 years old son arrested by Israeli soldiers at a checkpoint. The soldiers blindfolded him and took him to a nearby airport and started kicking him all over his body. Every half an hour, she would be told that her son will be killed and that she should be prepared. After two days living in terror and horror, Alia's child was released, but had tremendous psychological problems and disturbances the extent that Alia wished her son was injured or dead to reduce his current suffering.

Another case was of a woman participating in the research whose house seemed in good condition. However, during the interview and when asked about the frequency of consuming particular food items, the woman burst into tears. Her family had left Hebron, south of the West Bank and settled in Kalandia as her husband was working inside Israel; but he was later denied access to his work because of the Intifada and the Israeli refusal to give permits to Palestinian workers to enter Israel. Sixteen people were currently living in

the house. But as her husband became unemployed, they could only eat if the children searched in the garbage for pieces of iron and sold them to buy lentils or rice. These stories could continue as each woman in the camp has a different story but all were full of sufferings.

The living conditions of these Palestinian women should be considered as a significant component of the research as it influences their mental and physical health and these influenced the progress of fieldwork and their readiness to be involved in the research.

6.2 Preliminary Work

Preparation for the field work took place while the study protocol was developed in London and Palestine in 1997. This involved contacting the responsible authorities and health care providers to get their approval. The Palestinian Ministry of Health and UNRWA officials in the headquarters (Jordan) and the West Bank had been approached and had in principal agreed to the study. A copy of the study protocol was sent to them for final approval. Contacts were also made with officials from UNRWA regarding choice of survey areas and it was initially agreed in principal that three Palestinian refugee camp locations would be randomly selected: from the north, middle and south camps of the West Bank. But because of the political situation and the difficulty of movement to and from the different areas of the West Bank, and because of scarcity of funding, the study was conducted in two refugee camps in the middle of the West Bank: the Amaari and Kalandia refugee camps.

Contacts were also made with two research laboratories: one in Ramallah (the West Bank) and the other in Herzelia (Israel). The research laboratory in Ramallah is a member of the Randox International Quality Assessment Schemes in Haematology, Clinical Chemistry and Immunoassays, while that in Israel is an American Medical Laboratory under the continuous standardization programme of the CDC in the USA. The Ramallah laboratory was chosen for reasons mentioned above, as the mobility of goods and people was very difficult to and from Israel which would have affected the movement of blood samples to Israel.

Meetings were conducted with cardiologists, diabetologists and obstetric/ gynaecologists to emphasize the significance of conducting such a study in Palestine. Additionally, two

Palestinian universities were approached for possibilities of co-operation; Birzeit and Al-Quds universities. Finally, however, due to logistical and administrative issues, the fieldwork was conducted without their involvement.

6.3 Consultative Process

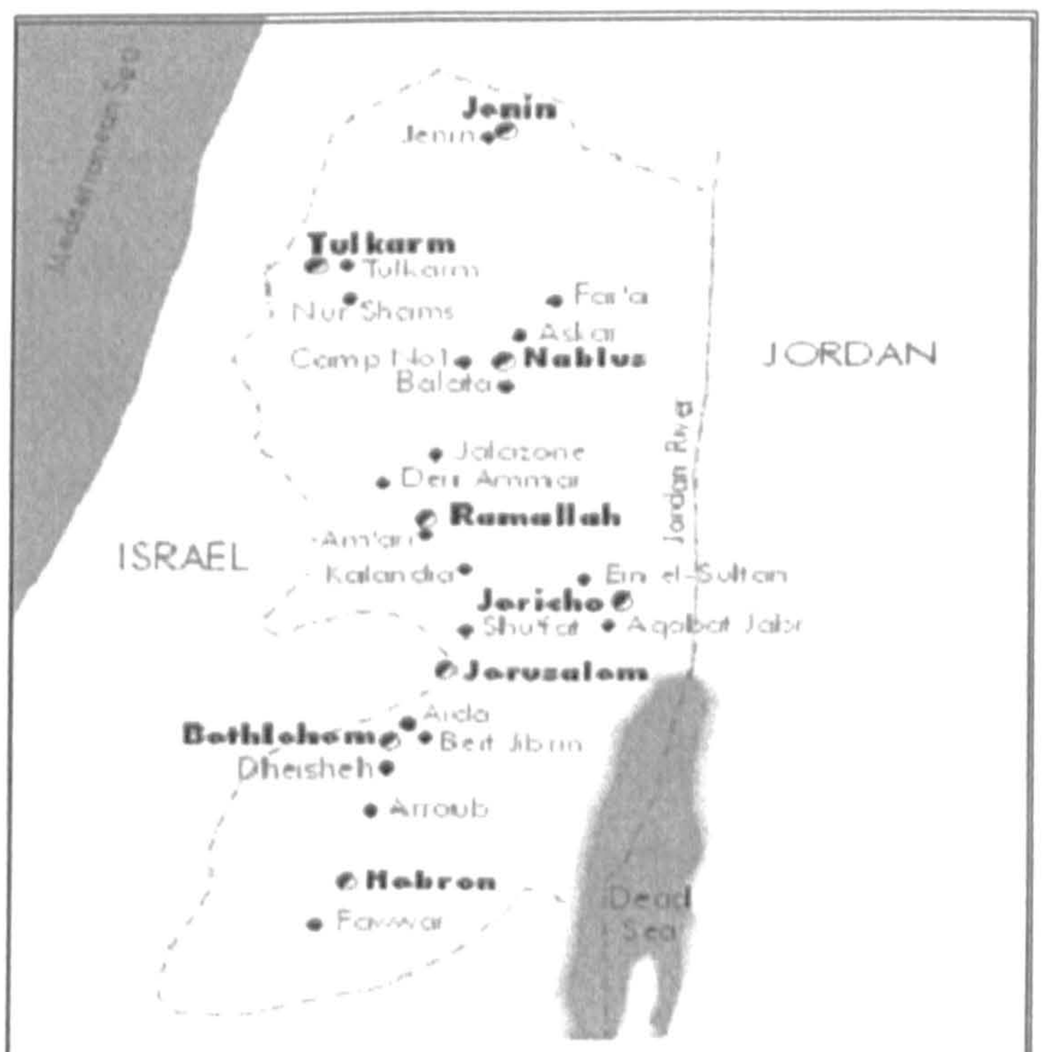
Co-operation and input was sought at various levels as an important step in implementing this study. Community advisory groups including both men and women from the Amaari and the Kalandia refugee camps were formed. Their initial role was to appoint a liaison person between the community and myself, the principal investigator. Later, their role included providing feedback results to the community and input in future programmes arising from the study.

A multi-disciplinary technical review group was also established, consisting of various professionals from the West Bank in the following fields: gynaecology/obstetrics, cardiology, diabetology and medical laboratory (see above). The role of this group was to review the methodology, provide written feedback and participate in a one day workshop to discuss the methodology and data collection instruments.

6.4 Study Setting

The study was conducted in two refugee camps, the Amaari refugee camp and the Kalandia refugee camp as Map 6-1 shows:

Map 6-1: The Location of Amaari and Kalandia Refugee Camps



Source: UNRWA, West Bank, 2005

6.4.1 Description of the Targeted Refugee Camps

6.4.1.1 The Amaari Refugee Camp

The Amaari Refugee Camp was established in 1949 on an area of 92 dunums (4 dunums= 1 acre), within the municipal boundaries of Al-Bireh city. By 1957, all tents in the camp had been replaced with cement block shelters. Like most of the West Bank camps, Amari suffers from overcrowding, poor sewerage and water networks. Following the redeployment of the Israeli army in 1995, the camp came under Palestinian Authority control.

The camp is about 18 km north of Jerusalem. The people in the camp came originally from different localities but the great majority lived in the coastal plain of Palestine. As of December 1995, the population of the camp comprised of 6500 individuals living in around 920 families. The average household size was about 7.1 persons per family. The population has since increased to 8805 registered refugee population (inhabitants) in 2005. The camp is severely overcrowded with cramped housing, unpaved streets and open sewers. UNRWA is responsible for the refugees in the camp. UNRWA provides health and education services, water and electricity supply, sanitation and building control. There is one health clinic in the camp which serves the camp inhabitants and an additional 22,000 people, who are largely refugees living outside the camp, basically in Al-Bireh and Ramallah cities. The clinic provides maternal and child health services, general medicine, dental services, a diabetes and hypertension clinic and laboratory services [257].

6.4.1.2 The Kalandia Refugee Camp

Kalandia Refugee Camp was established in 1949 on 353 dunums, 11 kilometers north of Jerusalem. The main Jerusalem-Ramallah road runs through the camp. The Israeli authorities consider this area as part of Greater Jerusalem, and the camp was excluded from the redeployment phase in 1995. Kalandia camp remains under Israeli control in "zone C". In 1997, the Israeli authorities resealed the main entrance to the camp, which had been previously sealed during the *Intifadah*, with large cement blocks, allegedly to prevent stone throwing at passing Israeli cars on the main road. The camp still witnesses clashes with Israeli soldiers with frequent stone throwing incidents.

The number of the registered Refugee Population in Kalandia refugee camp is 10,024. The clinic provided the same health services as the Amaari refugee camp [258].

6.5 Description of the Subject Population

6.5.1 Sample Size

This cross-sectional household survey of 515 Palestinian women aged 40-65 years, of any marital status, was conducted in the Amaari and Kalandia refugee camps. All women living in the two camps and aged 40-65 years were selected from UNRWA registration records, which cover the population living in refugee camps within the West Bank, UNRWA being responsible for the refugees in the camps. The figures of registered Palestine refugees are regarded as comprehensive demographic data, and they are updated regularly.

The original plan was to perform the study in the Amaari refugee camp only because it is very close to where I lived during the uprising and therefore gave me relatively easy mobility to and from the camp. But when I had identified the total number of women aged 40-65 in the UNRWA registration records living in the Amaari refugee camp, this came to 205 women. So after consultation with UNRWA staff and my supervisor, I decided to include Kalandia refugee camp as it is very close to the Amaari refugee camp, has almost the same environmental and socio-economic conditions but is larger. The total number of women aged 40-65 years in the Kalandia refugee camp came to 382 women and therefore the total number of women in both camps came to 587 women at the time the study was conducted in 2001. The names of these women were listed and they were assigned random numbers. Then these random numbers were put in a basket and a sample of 515 women was selected randomly from this basket.

6.5.2 Sample Size Calculations

At the time the study was planned, it was not certain which of the various CHD risk factors were of prime interest, or exactly which groups of women would be compared to demonstrate an effect of parity. Literature suggested that HDL-C (High Density Lipoprotein-Cholesterol) was likely to be an important factor and a change of 4.9mg/dl (0.13 mmol/L) would represent a sufficiently important gradation in risk (see below). To focus the sample size calculation on the comparison of two groups, a cut-point of parity 6, being reasonably close to median parity, was chosen.

HDL-C levels are inversely associated with CHD [259], and may be the best lipoprotein predictor of CHD in women [93, 260, 261]. HDL-C has shown a strong inverse relation to CHD in women in the Framingham Heart Study [262], and the Lipid Research Clinics Study [263]. In the Framingham study, a 1 mg/dl (0.03 mmol/L) increase in HDL-C was related to a significant 3% decrease in CHD risk, and in the Lipid Research Clinics Study, a 1 mg/dl (0.03 mmol/L) increment was associated with a 4.7% decrement in cardiovascular mortality rates. Kritz-Silverstein et al, [140] found that women with 5 or more pregnancies had HDL-C levels that were 4.9 mg/dl (0.13 mmol/L) lower than those with less than 5 pregnancies, and 4.0 mg/dl (0.10 mmol/L) lower than nulliparous women). This difference of 4.9mg/dl (0.13 mmol/L) was taken as clinically significant for risk of CHD [264] [259].

The following formula (comparison of two means) is needed for calculating the sample size: $(u+v)^2 \ (\sigma_1^2 + \sigma_2^2) / (\mu_1 - \mu_2)^2$

σ is the standard deviation of the distributions of HDL-C level in each group (parity 6+ vs. parity < 6). $\mu_1 - \mu_2$ is the assumed true difference in the means of HDL-C.

This formula is implemented in the STATA command sampsi,

To apply this formula, some idea of the likely sampling variation is required. In the reference quoted above, the difference of 4.9 is significantly different from zero, with t= 7.24. The SE can be calculated approximately from this as 4.9/7.24 which is 0.677. Given also the numbers in the groups being compared, the standard deviation is calculated as 12.4. The formula was then applied in a variety of possible scenarios; Table 6-1 below shows the results for these different scenarios:

Table 6-1 Different Scenarios for the sample size calculation:

$\mu 1-\mu 2$	2	3	4	5	2	3	4	5
Power	80	80	80	80	90	90	90	90
Significance level	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
σ (mg/dl)	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
Number of women in each group	600	266	150	96	804	357	200	129
Total number of women	1200	532	300	192	1608	714	400	258

The difference in the reference above is 4.9. However, to derive a sample size for this difference is to ignore the uncertainty in the value 4.9. It seems more reasonable to plan

to be able to detect a difference equal to the lower end of the confidence interval on 4.9. This is 3.6 (4.9 – 1.96*SE). With 90% power, the table suggests a sample size between 400 and 700 in the two parity groups combined. Using the formula for a difference of 3.6, suggests that 250 women are needed in each group, or 500 altogether. The 515 selected give a small margin for non-response.

6.6 Selection Criteria

6.6.1 Inclusion Criteria

Women aged 40-65 years living in both the Amaari and Kalandia refugee camps were included irrespective of their marital status. (See selection procedure, above). Current users of antihypertensive medication were included in the sample, but allowance for this medication was made later in certain statistical analyses. A similar strategy was used for women on diabetic medication.

6.6.2 Exclusion Criteria

Currently pregnant women and women aged less than 40 and above 65 years were excluded. Women who were currently breastfeeding or who had a pregnancy ending within the past 12 months were also excluded; and women who had not fasted for 12 hours were omitted from the blood tests.

6.7 Recruitment of Women

The selected women were sent a letter explaining the purpose of the project with an invitation to participate in the study. They were then approached individually by the principal investigator (I) and the community leader and a brief description of the study and its importance to women's health was explained. The women were asked to give their written consent before entering the study. Those who accepted the invitation were given a set of written and verbal instructions about all study measurements including preparation for blood tests. An appointment was set for a trained interviewer and the principal investigator, to visit the women at home and administer the questionnaire. Furthermore, information about the study objectives and its importance to women's health was disseminated through the community leaders, UNRWA officials and clinic staff, and women activists in the camps.

The 15 cases of non-responders (those who filled the questionnaire but refused to come to the clinic for the blood withdrawal and the laboratory tests), were invited repeatedly and after 3 reminders were contacted to fill in a brief questionnaire so as to identify their reasons for not attending and to assess whether they differed from participants. It emerged that 33.3% of these women were out of the country, 20% forgot to fast each time they had an appointment, and 46.7% could not bear the idea of giving a blood sample.

6.8 Definition of Exposure

Parity was defined as the total number of live births. Women were asked to report the total number of live births as well as other pregnancy outcomes (gravidity including abortions and still births). Parity was analyzed as both a continuous variable and a categorical variable. Women were grouped in five categories by number of live births (0, 1-3, 4-6, 7-9, and 10+). Parity 10+ was chosen as the baseline in the analyses relating parity group to CHD risk factors.

6.9 Definition of Outcome

Four groups of outcome variables were considered: obesity, lipids and lipoproteins, diabetes and hypertension. The categorical outcome variables obesity and abnormal lipid levels were defined according to WHO criteria [265] [266]. Diabetes was defined according to WHO criteria [266] [267] [268] . Hypertension was defined according to the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7) [269]. These outcome variables are defined more fully below, and were analyzed both as continuous variables and as categorical variables as appropriate.

6.9.1 Obesity

Three obesity indices were used in measuring body size and body fat distribution.

1. Body Mass Index (BMI; kg/m^2) was used to assess overall obesity.
2. Waist Circumference (WC; in cm) was used to assess central obesity.
3. Waist to hip ratio (W/H ratio) was used to assess abdominal obesity.

Overall obesity was defined by using the Body Mass Index (BMI) classification suggested by the WHO expert committee [265] see Table 6-2. BMI is a measure of the weight in kilograms divided by the square of the height in meters (kg/m^2).

Table 6-2 Body Mass Index Classification

BMI (weight/height$^{2)}$(kg/m^2)	Clinical Classification
Lowest-18.49	Chronic energy deficiency
18.5-24.99	Normal
25.0-29.99	Overweight
30.0-39.99	Obese
40.0-highest	Severely obese

Overweight women were defined as having BMI between 25.0 and 29.99 kg/m^2. Obese women were defined as having BMI $\geq$ 30.0 kg/m^2.

Waist circumference is considered as a suitable indicator of central adiposity, and a surrogate of visceral adipose tissue in adults.[270]. Increased waist circumference, a value $\geq$ 88 cm in women indicates intra-abdominal fat, indicating central obesity.

Abdominal adiposity: The waist to hip ratio (WHR), defined as waist circumference (cm)/ hip circumference (cm), is considered as a useful index for describing quantitatively adipose tissue distribution [265]. WHR $\geq$ 0.85 is generally considered indicative of an android fat distribution and abdominal obesity. Women with WHR $\geq$ 0.85 can be significantly at increased risk of developing CHD and Type II diabetes [271].

Throughout the thesis, I have used WC $\geq$ 88 cm as indicative of central obesity and W/H ratio $\geq$ 0.85 cm as indicative of abdominal obesity. In summary: overall obesity was defined as BMI $\geq$ 30.0 kg/m^2; central obesity or adiposity was defined as WC $\geq$ 88 cm and Abdominal adiposity was defined as WHR $\geq$ 0.85 cm.

6.9.2 Lipids and Lipoproteins

For plasma total cholesterol, HDL-C, LDL-C and Triglycerides, the WHO criteria for the choice of "cut-point" lipids and lipoprotein levels was followed as indicated in Table 6-3.

Table 6-3 WHO Criteria for Lipids and Lipoproteins [257]

Definition	Value
Elevated Cholesterol	> 5.2 mmol/L (200 mg/dl)
Elevated LDL-C	> 3.5 mmol/L (135 mg/dl)
Elevated Triglycerides	≥ 1.7 mmol/L (150mg/dl)
Decreased HDL-C	< 1 mmol/L (40 mg/dl)
A ratio of T-Chol/ HDL-C	> 0.13 mmol/L, (5 mg/dl)

Quantitative values of these outcomes were also used in the statistical analysis

6.9.3 Diabetes

Diabetes mellitus is defined internationally as fasting plasma glucose of 126 milligrams per deciliter (mg/dl) or more, which is ≥ 7.00 mmol/L; or a history of physician diagnosed diabetes with or without current use hypoglycaemic agents. Fasting is defined as no calorific intake for at least eight hours.

Impaired fasting glucose is defined as 110 to 125 mg/dl (6.1 to 7.00 mmol/L). This denotes "pre-diabetes" as a condition in which blood glucose levels are higher than normal but not yet diabetic, 6.1 to 7.00 mmol/L, (110-125 mg/dl). Women with no history of diabetes and whose plasma levels do not meet the above criteria are considered as non-diabetic.

Table 6-4 WHO Criteria for Diagnosis of Diabetes Mellitus [257]

Definition	Value
Fasting plasma glucose or on medication	≥ 7.0 mmol/L (126 mg/dl)
Impaired fasting glucose (Pre-diabetic)	≥ 6.1-7.00 mmol/L (110-125 mg/dl)

Quantitative value of fasting blood sugar was also used in the statistical analysis.

6.9.4 Hypertension

High systolic blood pressure was defined as a mean systolic blood pressure ≥140 mmHg and/or on medication. High diastolic blood pressure was defined as a mean diastolic blood pressure ≥90 mmHg and/or on medication. Hypertension was defined as having a mean systolic blood pressure ≥140 and/or a mean diastolic blood pressure ≥90 mmHg or taking antihypertensive medication [269] [272] [1] . Quantitative values of systolic and diastolic blood pressure were used in the statistical analysis.

Additional analysis were performed with women's report of coronary heart disease as an outcome variable, the metabolic syndrome as another outcome variable and the 10 years Framingham risk score as a third outcome variable in order to evaluate the risk of coronary heart disease the women might face. Definitions of these additional outcome variables as well as other covariates are shown in Appendix 2.

6.10 Data Collection Methods and Instruments

The data collection in this study consisted of a structured interview divided into health status, life style and reproductive health risk factors, plus blood pressure and anthropometric measurements and blood samples.

6.10.1 Health Status, Life Style and Reproductive Health Risk Factors Questionnaire

A standardized face to face interview using a structured questionnaire was employed in the home. The questionnaire was translated into Arabic by the principal investigator and the responses translated back into English. The questionnaire included the exposure variable of interest and other variables that were potential confounders or covariates potentially to be controlled for in the analysis. These included the demographic and socio-economic status of these women (age, education of women and their husbands, marital status, employment, occupation of women and their husbands, income sources, housing condition and crowdedness, possession of household amenities such as an automatic washing machine and a car); their lifestyle risk factors (smoking habits, passive smoking, physical activity, hours watching TV and assistance in housework as proxy to physical activity, stress status and dietary patterns); and their reproductive health associated factors (age at menarche, age at first marriage, age at first pregnancy, and age at first live birth, parity, gravidity, history of miscarriages, pregnancy terminations, breastfeeding, age at menopause, hysterectomy and/or removal of one or two ovaries, use of oral contraceptives, use of hormone replacement therapy, regularity of menses, and history of infertility). In addition, questions on health status, medical history and use of medication as well as the family history of chronic diseases were included. For more details of the questionnaire, see Appendix 3.

No questions were asked on alcohol consumption, as this is not culturally appropriate especially as women participating in the study were all Muslims, and were unlikely to consume alcohol anyway.

The dietary data and all nutrition related data was not used in the analysis following the recommendations of the upgrading panel and time constraints. This data will be looked at in subsequent analysis and reports.

6.10.2 Interviewer Selection and Training

Four female interviewers (two from each camp) were selected based on motivation and interest as well as their ability to follow instructions and conduct the interviews exactly according to the protocol. Other selection criteria included good communication skills, completion of at least high school, knowledge of the local community, and preferably being a camp resident.

The selected interviewers were trained by the principal investigator in questionnaire interviewing techniques, questionnaire completion, accuracy verification, and handling problems usually encountered in the field. Interviewers worked in pairs as it was more culturally appropriate. It was expected that they would complete 4 questionnaires per day, though this was not usually met due to curfews and Israeli invasions in the two sites.

The questionnaire was pilot tested as described below (section 6.12).

6.10.3 Blood Pressure Measurements

Blood pressure was measured with a mercury sphygmomanometer, after at least 5 minutes of rest, in a sitting position by a trained nurse according to a standardized study protocol. Blood pressure was recorded in mmHg. Two seated blood pressure measurements were averaged to obtain mean systolic and diastolic blood pressures. For more details on blood pressure measurements, see Appendix 4. The interview nurse recorded information on participant's current medication. Women were informed about the results and in case of a problem; they were referred to the UNRWA general practitioner for further medical advice.

6.10.4 Anthropometric Measurements

Anthropometry covered weight, height, waist circumference, and hip circumference. All anthropometric measurements were taken according to standardized instructions based on the recommendations of WHO consultancy groups [273] [265]. The reproducibility

of the anthropometric measurements (intra-observer) was assessed at the beginning of the study. Repeated reproducibility checks were conducted every day for standardization and correctness of the instruments.

Body Mass Index (BMI)

Weight and height measures were recorded by the principal investigator with the subjects wearing very light clothing and without shoes. Body weight was measured to the nearest 0.1 kg using a balance scale. Women were asked to remove their shoes and heavy outer clothing, stand upright on the centre of the scale without touching any object, and the weight was recorded. Body height was measured with a stadiometer to the nearest 0.1 cm. Women were asked to stand erect against the wall, with feet parallel and heels, buttocks and back of head touching the wall behind them. The head was held straight looking forward, arms hung loosely at the sides. The head piece of the stadiometer was gently lowered, crushing the hair, making contact with the top of the head and the measurement was read. BMI was calculated as weight in kilograms divided by the square of the height in metres, weight/height^2 (kg/m^2).

Waist-Hip Measurements (W/H Ratio)

The waist and hip measurements were recorded by the principal investigator as well. Women were asked to stand relaxed. The principal investigator knelt at an appropriate height in front of the woman surveyed. Waist circumference was measured to the nearest 0.5 cm at the level midway between the lower rib margin and the iliac crest using a flexible tape measure (dress-maker's measuring tape).

Hip circumference was measured in the same way at the widest point between the iliac crest and buttock. The circumferences were measured with women standing. The Waist Hip Ratio (WHR) was calculated as waist circumference divided by hip circumference. Two measurements were taken for each parameter and if there was a difference between the two (more than 0.5 kg for weight and more than 1 cm for height, waist and hip) a third measure was recorded.

6.10.5 Blood Samples: Blood Specimens' Collection, Handling and Processing

Blood samples were taken in the clinic lab between 8.00 am and 11.00 am after an overnight fasting of 12 hours, by a trained lab technician. The period of fasting was

ascertained by questioning the women prior to registration for the blood sample. After registration, 10cc of fasting venous blood were collected from all women. Part of the blood was drawn in sodium fluoride tubes for the estimation of fasting blood sugar and the other part in plain tubes for lipids (Cholesterol, Triglycerides, HDL, and LDL) and insulin assays. All labelled test tubes were put in ice boxes and sent within one hour to the laboratory in Ramallah for analysis. In the laboratory, plasma was separated from blood cells by centrifugation. Fasting blood sugar and lipid profiles were estimated immediately. All different lipid parameters (T-cholesterol, HDL-C, LDL-C and triglycerides) as well as glucose assay were measured using enzymatic techniques. The Elisa technique was used for the insulin test.

Specific lipid controls were used for the quality control when performing lipid tests (lipid high and lipid normal), and regular control (high and normal) for glucose test. The controls and reagents used were ordered from the same manufacturer. For the insulin test, plasma samples were frozen and the tests carried out at least twice a week depending on the number of samples that were collected. Quality controls were carried out with each run.

6.11 Data Collection Logistics

6.11.1 Interviews

On the day of the appointment, the two female trained interviewers introduced themselves, obtained informal consent and collected information on several demographic and socio-economic variables, detailed reproductive and gynaecological histories, use of oral contraceptives and hormone replacement therapy, medical and family history, smoking habits, exercise, diet and dietary patterns. Information on current use of medication such as antidiabetic and antihypertensive medications was also collected. To avoid information bias, neither the interviewers nor the participating women were informed about the study hypotheses. Women were asked to go the next morning to the UNRWA clinic for blood withdrawal. They were given instructions about how to be prepared for blood testing and overnight fasting. Those women who could not make it for one reason or another, they were given another chance and another appointment for blood testing. If that particular evening was not a good one for fasting, the woman was given another appointment that would be convenient for her.

6.11.2 Biochemical Analysis of Blood Samples

Upon arrival at the UNRWA clinic, the research nurse registered the women and directed them to the laboratory where a medical laboratory technician took fasting blood samples for glucose level, total cholesterol, LDL-C, HDL-C, triglycerides and plasma insulin.

6.11.3 Blood Pressure Measurements

Women were then asked to go to the other room where the research nurse who has been trained in using a standard mercury sphygmomanometer measured their blood pressure.

6.11.4 Anthropometric Measurements

In the same room body weights, heights, waist and hip circumferences were measured with women wearing light clothing and without shoes, by the principal investigator.

6.12 Pilot Study

A pilot study of one month duration tested the feasibility of the study protocol (data collection methods and instruments). The questionnaire was pilot tested on women who were from the Amaari and Kalandia camps, but were not part of the study, in order to test the acceptability and clarity of the questionnaire to women.

Particular attention was paid to the recruitment and response rates of women who were invited for laboratory investigation as well as filling in a questionnaire. The pilot study sample consisted of 11 women from the Amaari refugee camp and 19 women from Kalandia refugee camp.

6.13 Ethical Considerations

The study objectives and protocol were explained to all women prior the study by UNRWA officials and the principal investigator. Informed consent for performing interviews and drawing blood samples was obtained. When cases were identified among women, they were informed about the results of the tests and they were referred to UNRWA clinic in the camp for further investigation and free of charge treatment. All women participating in the study were informed about the biometric results.

Consent of the ethics committees at the London School of Hygiene and Tropical Medicine and at the appropriate local centres including UNRWA was obtained. Women's names selected from UNRWA registration records, which were confidential records, were coded to ensure confidentiality. Names were replaced with a numerical identifier. All study procedures including the laboratory tests that were performed, the administration of the questionnaire, and ensured privacy of women participating in the study as stated in the data collection logistics section. All names were removed from fill-out questionnaires and laboratory results, and were coded numerically. For informed consent, please see next section.

All personnel involved in the study (the interviewers, the nurse, and the lab-technician) were supervised directly by the principal investigator who had good experience with data collection methods.

6.14 Informed Consent Procedures

Three types of informed consent procedures were employed: a first informed consent form that was presented to women indicating the purpose of the study and participation implication (Appendix 5), a second form was prepared by UNRWA detailing again the importance of the study and presenting me as the researcher performing the study on women's health (Appendix 6). Finally, a third consent form was signed by participants indicating their acceptance to be volunteers in the study under the supervision of the principal investigator (me). The form also explained that the study has been defined and fully clarified to participants by UNRWA's medical officer and the principal investigator (Appendix 7).

6.15 Statistical Details of the Study

6.15.1 Data Entry and Data Management

During the fieldwork phase, all questionnaires were checked and edited daily by the principal investigator. All data which were generated through the interview, body measurements, blood pressure measurements as well as laboratory measurements were entered using an Access 2000 programme prepared by an expert in data entry. The data entry programme included a number of characteristics such as:

- Reproduction of the questionnaire on the computer screen.

- Rules for logical and consistency checks on the data.
- Possibility for internal editing of answers.
- Maintaining a minimum of digital data entry and field work errors.
- User friendly handling
- Possibility of transferring data to a data analysis platform such as SPSS or STATA.

Data was entered once by the same person. Then all data entered into the computer was cleaned and checked by the principal investigator for further errors and missing data. The questionnaires were subjected to standard quality control procedures in terms of editing and coding with the help of a specialized person who reviewed the questionnaires again with the principal investigator.

6.15.2 Data Coding and Statistical Analysis

6.15.2.1 Statistical Analysis

The data was analyzed using the STATA 9 for Window statistical package and SPSS 14. Different statistical approaches were used to assess the relationship between parity and coronary heart disease risk factors (obesity, lipids and lipoproteins, diabetes and hypertension) as well as reported CHD, the metabolic syndrome and the 10 years risk of developing a CHD. The primary exposure of interest, parity was analyzed as a categorical variable with several categories (0, 1-3, 4-6, 7-9, and 10+) and as a continuous variable. The outcome variables of interest were analyzed both as continuous and as categorical variables as appropriate.

Descriptive Analysis

The distribution of each variable was examined to get a good understanding of the characteristics of the study population with respect to the exposure and other variables measured. Simple cross-tabulations were then produced. Categorical variables were summarized by grouping data appropriately and calculating frequency distribution. Continuous variables were summarized by calculating means and standard deviations. Continuous variables with non-normal distribution were summarized using the log-transformation. Risk of a particular outcome was calculated as a proportion.

Bivariate Analysis

Bivariate analysis was performed to identify associations and differences and to facilitate interpretation of the results. Three approaches were used. The first approach

incorporated each outcome variable as a binary variable and parity as a categorical variable. Comparisons of the percentage of the outcome variables among women of different parity groups were assessed by the chi-square test and the use of logistic regression. This approach made no assumptions concerning linearity of the relationship of outcome with parity, in contrast to the next two approaches.

Secondly, logistic regression on parity as a continuous variable was carried out. The change in odds of the outcome variable per extra child (unit change of parity) was estimated. This approach was used in some of the papers reviewed in the discussion section, and its inclusion here permitted a direct comparison of results.

The third approach took those of the outcome variables which were measured as continuous variables and the exposure variable (parity) with both variables being continuous, using a scatter diagram and by ordinary regression. The regression coefficient showed the estimated change in the outcome variable for a unit change in parity. The line of the scatter diagram also indicated the line for regression of the outcome variable on parity unadjusted. If the scatter diagram suggested a curved relationship, then testing for curvature (J-shaped or U-shaped) was applied by adding a quadratic term.

To account for the fact that some participants were taking medication for diabetes (n=77), and hypertension (n=111) at the time the CHD risk factor measurements were taken, censored regression models were fitted for fasting blood sugar and blood pressure which censored the outcome measure of those on medication at the observed value so the true value is assumed to be that observed or higher. So, when not on medication, the value for fasting blood sugar and mean SBP and DBP is taken as correct and exact, while when on medication the value for the outcome variables is taken as a minimum (that is, it is assumed the medication has reduced glucose level to some extent, although how much is not known).

Multivariate analysis

Multivariate analysis was used to examine the associations between parity and CHD risk factors with allowance for confounders (age, education of both women and their husband's and marital status) and other covariates (mediators such as assistance in housework, BMI, etc) These mediators were introduced one by one into the confounder-

adjusted model, using logistic regression for the categorical (binary) outcomes and multiple linear regression for the continuous outcomes, with parity taken as a continuous (not grouped) variable.

The details of the confounders and other covariates are given below.

Confounding and mediation

Additional variables, as well as parity, in the multivariate analysis were either confounders or mediators, as follows:

A confounder is a variable that distorts the association or the relationship between an exposure and an outcome.

In order for a variable to act as a confounder, it must be:

1. A risk factor for the outcome (predictive of disease occurrence);

2 A risk factor for the exposure, in fact it must come before the exposure;

3. Not on the causal path between the exposure and the outcome variable.

We have chosen the confounders in this study by applying this definition. Accordingly, the confounders of interest that meet the above criteria are age, women's education, husband's education and marital status. Adjusting for confounders in the association between an exposure variable and an outcome variable reduce the bias in the results.

Mediation: Not every factor that is associated with both the exposure and the outcome is a confounding variable. Other factors could be mediating variables. A mediator is also associated with both the independent and dependent variables, but may be part of the causal chain between the exposure and the outcome.

The confounding and the mediation effects cannot be distinguished on statistical grounds in the analysis of cross-sectional data. They can only be separated from each other based on the understanding of the total disease process.

For example, the mediator "assistance in housework" reduces the association between the exposure (parity) and the outcome (obesity). However, we should not conclude that parity is less a real cause of obesity, because assistance in housework as a proxy to physical inactivity may be part of the causal pathway from parity to obesity. So the mediator is along the causal pathway between parity and obesity.

***Multiple testing*:**

A large number of statistical tests are expected to be carried out for the several outcomes variables. There is always a chance of getting false positives when doing multiple

statistical tests. If one carries out one test and set the p value at 0.05 level, then the chance of getting a significant result when there is no underlying effect is 1 in 20 or 5%. So a significant result is still possible if actually there is no effect with this chance, and this would be a false positive result. When doing several tests, this applies to each one. So doing several tests and accepting significant results as indicating an effect, one might go wrong more often than the p-value suggests and the chance for one or more false positives will be greater.

One can use a statistical strategy to get around this and the one often quoted is the "Bonferonni Correction". When this is used, results are accepted as significant only when the P-value of the test is much smaller than the usual 0.05. It is calculated by dividing 0.05 by number of tests. In our study, this approach would be difficult to apply, as we are not sure how many tests will be carried out, it must be more than 100 and at this stage it is hard to plan for. But, even if we adopt it and accept as statistically significant only those effects that get a very small P-value, then the power to detect an effect that does exist is much reduced and the study as a whole is weakened.

In summary it is not a good idea to rely only on statistical tests to show if an effect exists or not; rather one must use the P-value as contributing to the strength of evidence for an effect. One must look for the combination of the evidence from the P-value with other evidence such as the findings from other studies in the literature that have shown evidence for the effect and from applying what is scientifically known about the plausibility of the effect. This broadly is the approach adopted here.

6.16 Quality Assurance and Quality Control

Quality assurance and quality control activities were performed at all the different phases of the study in order to maximize the reliability and validity of the data collected. The field workers recorded the responses on to the questionnaires at the households. They then reviewed the questionnaires and the principal investigator also reviewed the questionnaires with the field workers at the site, on a daily basis, then filed and stored them at home. The nurse filled in the blood pressure measures and the principal investigator filled in the anthropometric measurements at the time the women came to the clinic on appointment. The laboratory technician recorded all the lipid profiles as well as the fasting and plasma insulin results on official laboratory forms. The principal investigator received the forms at the end of the week and after checking and reviewing the lipid, insulin and sugar profiles for any inconsistencies, the principal investigator

transferred the data from the official laboratory forms to the questionnaires before it was entered into the computer programme.

The quality control of the forms and questionnaires were carried out routinely throughout the period of the field work. Cross checking of information was frequently made by the field workers and the nurse under the supervision of the principal investigator. If inconsistencies were detected and could not be resolved by the field workers at the site, then they were requested to repeat checking the questionnaire with the subject to correct or complete it as appropriate.

In addition to the initial training programme, the fieldwork team had regular meetings with the supervisor (I), who was the principal investigator of the study, during the whole period of data collection, in order to share experiences and discuss difficulties encountered in the work. All equipment used in this survey was checked to ensure quality results of the measurements.

Quality control of laboratory analysis was performed according to established programmes, based on the scientific standards of the laboratory involved in the analysis. Before submission to keyboard data entry, the questionnaires were reviewed for completeness, consistency and other errors. After data entry, computer programmes were run to verify the consistency of responses within each questionnaire and between them.

Chapter 7
DEMOGRAPHIC, SOCIO-ECONOMIC AND HEALTH CHARACTERISTICS OF WOMEN SURVEYED

Chapters seven to thirteen discuss the actual results from the data analysis. The first five sections of chapter seven describes the general demographic, socio-economic, and health characteristics of the women surveyed in the Kalandia and Amaari refugee camps. Section 7.6 describes the prevalence of principal characteristics by parity groups and section 7.7 describes the mean and standard deviation of coronary heart disease risk factors by parity groups.

7.1 Demographic Characteristics

A total of 515 women from the Amaari and Kalandia refugee camps participated in the study. Their age ranged from 40 to 65 years, with a mean of 49.4 years. The majority were married and living with their husbands, (Table 7-1)

The basic socio-demographic characteristics are shown in Table 7-1. Since the refugee camps are very populated, around 45% of the women lived in cramped houses, where the average family size is 7.43 with a maximum of 30 people. Around 50% of them were born in the camps and had been living there ever since. Thirty-four percent were born inside Mandatory Palestine, but were forced to migrate with their families after the Arab Israeli war in 1948 and had lived since then in these refugee camps, assuming that one day they will go back to their homeland.

Table 7-1: Socio Demographic Characteristics of the Study Population

Socio Demographic Characteristics		
Number of women participating in the study	515	
Variable name	**N**	**Mean (SD), or %**
Age of women in categories, %	**Frequency**	**Percent (%)**
< 45	159	30.9
45 – 49	115	22.4
50 – 54	110	21.4
55- 59	95	18.5
60 +	35	6.8
Total	**514**	**100**
Mean age in years	514	49.4 (6.43)

Marital status, %	Frequency	Percent (%)
Single	21	4.1
Married	382	74.2
Divorced	17	3.3
Separated	11	2.1
Widowed	84	16.3
Total	**515**	**100**
Family size		
Number of people living in the household (average family size)	512	7.43 (3.89)
Place of birth, %	**Frequency**	**Percent (%)**
Jerusalem	34	6.6
West Bank	256	49.7
Gaza Strip	24	4.7
Palestine 1948	173	33.6
Arab Countries	26	5
Other Countries	2	0.4
Total	**100**	**100**
Mean number of years lived in the camps	515	33.7 (13.15)

7.2 Socio-Economic Status

7.2.1 Education

The women had a mean of 5.62 years of education. Twenty-three percent had no formal education, in comparison to 38.6% with elementary education, 32.4% with secondary education and only 5.8% with higher education, (Table 7-2). This low number of better educated women is probably due to early marriage being common, as well as the social and economic constraints obliging parents to favour marriage over education. Around 47% of women surveyed were married below 18 years of age, of whom 23.7% were married at an early age below 16 years.

7.2.2 Occupation

Women's participation in the labour force was low and the vast majority (84.7%) were unemployed. Out of the 79 women employed, 20.3% were unskilled workers and 31.6% worked in small private businesses. Following the Palestinian uprising and due to movement restriction and checkpoints as well as curfews, many people, both men and women, lost their jobs in Israel and became unemployed. This situation has compelled families living in the camps to establish their own small private businesses as an alternative to losing their jobs. However, these businesses are very small.

This low participation of women in the labour force does not however accurately reflect women's economic contribution as a working force since the formal definition of "employment" excludes household work performed by women. This is unpaid and therefore seen as unproductive despite the fact that many hours are spent in such tasks in food production and clothes making, all of which produce consumable items and contribute directly and indirectly to the welfare of the family [14].

Women's participation in the labour force is limited by a variety of factors including this lack of job opportunities, low levels of education, high fertility rates and early marriage. There is no comprehensive community support system that encourages women to work beyond household work, as there is a lack of quality kindergartens or nurseries, day-care centres for the elderly or other facilities that would liberate women from some of their many household responsibilities.

Around 49% of the husbands were employed, of which 31% were unskilled workers, while another 30% worked at UNRWA. Most of the women interviewed depended on salaries of employed household members as their primary source of income. As indicated in Table 7-2, 46.3% of the families have one member currently working, 27.5% have two and 8.9% have three family members currently working. However, around 14% of households have none of their members working.

Table 7-2: Education and Economic Status of the Study Population

Years of schooling in categories, %	**Frequency**	**Percent (%) or mean (SD)**
No formal education	119	23.1
Elementary	199	38.6
Secondary	167	32.4
Higher	30	5.8
Total	**515**	**100**
Mean years of schooling	515	5.62 (4.29)
Currently employed, %	79	15.3
Occupation, %	**Frequency**	**Percent (%)**
Unskilled worker	16	20.3
Skilled worker	14	17.7
Employee	24	30.4
Private business	25	31.6
Total	**79**	**100**
Husband's years of schooling, %	**Frequency**	**Percent (%)**
No formal education(0)	85	17.7
Elementary (1-6)	166	34.7

Secondary (7-12)	170	35.5
Higher (12+)	58	12.1
Total	**479**	**100**
Mean Husband's years of schooling	479	6.87 (4.67)
Husband's currently employed, %	241	48.8
Husband's occupation, %	**Frequency**	**Percent (%)**
Unskilled labour	75	31.1
Skilled Labour	36	14.9
Employee	56	23.2
International organization	73	30.3
Private business	1	0.4
Total	**241**	**100**
Number of people working in the household	**Frequency**	**Percent (%)**
0	69	13.7
1	234	46.3
2	139	27.5
3	45	8.9
4	8	1.6
5	10	2
Total	**505**	**100**

7.2.3 Wealth Status

In order better to assess the financial situation of the families interviewed, questions were asked pertaining to household amenities, real estate and landholdings. In general, people were unwilling to respond frankly to questions directly related to property and income, in part because this discussion is culturally sensitive, but also because many of them fear that the information will somehow reach the ears of the tax collector and cause them problems. Hence, the information gathered in the course of this survey with regard to household amenities and property may not be completely accurate, but ownership of certain appliances can reflect overall economic status to a certain degree (e.g., owning a deep freeze, clothes drier, microwave oven, satellite dish and /or private car can be relatively sound indicators of the family's financial status). Within this framework, we have created a variable called the family affluence scale where we have combined possession of amenities and household crowdedness to reflect a fair distribution of wealth among families. Details are found in Appendix 2.

In general most people living in the camps are more or less similar in their socio-economic status. Those who become financially better off try to move to the outskirt of

the camp and those who are ever better off might live in cities such as Ramallah and Al-Bireh where they can still have access to all UNRWA services but have a better quality life. It is interesting to note that although the majority of households own a house (89.9%), a coloured television (94.6%) and a fridge (95.9%) as shown in Table 7-3, these do not actually reflect entirely the wealth of a family since the status of the house and its' space as well as the condition of other available utilities determine more the family's wealth. Moreover, refugee population houses used to belong to UNRWA but were offered later to them as a temporary arrangement leaving the refugees with small houses built with low quality material. Forty-five percent of families interviewed lived in definitely crowded conditions and 34.6% lived in moderately crowded conditions as shown also in Table 7-3.

Table 7-3: Distribution of Amenities at the Household and the Crowding Scale

The availability of some amenities at the household, %	Frequency	Percent (%)
Number of women	**515**	
Own house	463	89.9
Coloured TV	487	94.6
Video	152	29.5
Fridge	494	95.9
Deep freeze	24	4.7
Full automatic washing machine	115	22.3
Clothes dryer	19	3.7
Dish washer	11	2.1
Microwave	47	9.1
Air condition	9	1.7
TV satellite	153	29.7
Private car	91	17.7
Crowding Scale, % [1]	**Frequency**	**Percent (%)**
Crowded	231	45.2
Moderate	177	34.6
Not Crowded	103	20.2
Total	**511**	**100**
Family Affluence Scale (FAS), %	**Frequency**	**Percent (%)**
Poor	225	43.7
Average	164	31.8
better off	126	24.5
Total	**515**	**100**

[1] Based on the number of persons per room; crowded is 1 or less, moderate crowding is between 1 and 2 and not crowded is more than 2.

Taking all the above mentioned indicators into consideration, the family affluence scale reveals that 43.7% of households are poor in comparison to 31.8% of average status and 24.5% are better off as indicated in Table 7-3.

7.3 Reproductive History of the Women

7.3.1 Early Marriage

Around 59% of women, all of whom were ever married, had married young, below or at the age of 18 years (the minimum age at first marriage was 11.5 and maximum age was 41 years). Of these 23.7% married early, below 16 years of age, as shown in Table 7-4

This relatively high rate of early marriage is due largely to custom and to the economic and social constraints which oblige parents to marrying their daughters in order to lessen household expenditures. In addition many families believe that their daughters, once they are married, will be safe from any temptation to "deviant" or societal unacceptable behaviour.

Early marriage forces young women to assume parental responsibilities at a time they are growing and need supervision. The mean age at first birth in this study was 20.1 years with a median of 19.2 years. Table 7-4 presents age at first birth and indicates that 13.5% of women had their first birth when they were less than 16 years old.

There was little practice of birth spacing. Frequent births can adversely affect overall health of women. Mean age at menarche was 13.4 and mean age at menopause was 48.2 years.

7.3.2 Number of Births and Pregnancies

Palestinian families in the West Bank and the Gaza Strip have a high annual birth rate. The crude birth rate in 2006 was 36.7 (41.7 in Gaza Strip and 33.7 in West Bank) per 1000 population [17]. The fertility rate in 2006 was also high at 4.6 births per woman (5.4 in the Gaza Strip and 4.2 in the West Bank) [18] [19]. Not only do Palestinians marry young, but their traditional values favour large families, as children are thought to help maintain the wealth and support system of the family. In addition, the political environment (the Intifada and the death of so many male children) has created in people a sense of responsibility about contributing to the population.

The number of children per woman ranged from 0 to 21. The women surveyed were found to have born on average 7.3 live children in their lifetime (median 8). The survey was carried out in 2001, 4 years before 2005, and "captured" fertility over several decades before that time. The mean number of pregnancies the women ever had was 8.86 (median 9). Sixty one percent of the women surveyed had 7 or more children, and only 8.1 % had no children at all. This small group of parity 0 consisted of 42 women out of whom 21 were single, 11 were married and living with their husbands, 4 were divorced and 6 were widowed. In Palestinian culture, women have little choice of not becoming pregnant as it is not widely accepted in the society. So beside the 21 single unmarried women, 15 out of the other 21 were most probably either infertile or their husbands were infertile. On this basis, probable infertility among the parity 0 group was 28.3% compared to infertility among the study population which was 8.7%. In general, Palestinian women do not have a say on how many children they will have or on their birth spacing. Society, relatives and husbands exert enormous pressure on women regarding the number of children, not taking into consideration the huge burden that large families impose, or whether women concur or not. Maternal mortality and morbidity is not yet an aspect given importance by health policy makers, despite the value placed on the woman's role as a mother.

Table 7-4: Reproductive History of Women

Variable name	N	Mean (SD) or %
Age at first marriage in years, %	**Frequency**	**Percent (%)**
<16	117	23.7
16-18	174	35.2
> 18	203	41.1
Total	**494**	**100**
Mean age at first marriage	494	18.8 (4.6)
Mean age at first pregnancy, years (min 13.17 & max 42.08)	477	19.37 (4.29)
Age at first birth in years, %	**Frequency**	**Percent**
< 16	64	13.5
16 – 18	109	23
> 18	301	63.5
Total	**474**	**100**
Mean values of further variables		
Age at first birth, years	474	20.09 (4.26)
Age at last birth, years (min age 16.50 and max 49)	469	35.5 (5.03)
Number of children women ever had (parity)	515	7.30 (3.69)
Number of pregnancies women ever had (gravidity)	515	8.86 (4.56)
Pregnancies ended as a miscarriage or abortion	313	2.40 (1.88)
Pregnancies ended as still birth	65	1.31 (0.61)
Age at menarche, years	508	13.36 (1.39)
Age at menopause, years	229	48.19 (5.45)

Variable name	N	Mean (SD) or %
Years since last birth	469	15.4 (6.04)
Fertility related variables		
Number of women	515	
History of infertility, %	43	8.70%
Periods stopped,%	229	44.6%
Ever use oral contraceptive pills, %	208	40.4%
Ever use Hormone Replacement Therapy (HRT), %	6	1.2%
Polycystic ovaries,%	13	2.6%

7.4 Health Status

7.4.1 Women's General Health Status

In spite of the fact that 48% of women described their health as being good, another 43% described it as being average or below. The burden of large families leads to women not putting their health as a first priority, as Palestinian women tend to place the health needs of their children and husbands before their own [14]. They tend to minimize the importance of any adverse health conditions they have. This is partially due to their cultural upbringing where "girls are taught to endure physical pain and suffering especially that related to reproductive functions, in menstruation, pregnancy, and child-birth, since this related to fertility, which is the overriding symbol by which women gain their socio-economic status within the family and the community at large" [274]. In addition to their daily workload and caring for the children, once they become grandparents, they focus their energy in turn on their grandchildren.

When women were asked whether they ever had a cervical smear test and a mammogram X-ray test, only 20% reported a smear test and 8% a mammogram. Twenty percent reported they had had their triglyceride measured while 31.8% reported they had their cholesterol level measured during their lifespan. Around 40.4% of women had ever used the contraceptive pill, and 1.2% ever used HRT.

7.4.2 Family History of Certain Diseases

When women were asked about family history of diseases, 40.6% had a family history of hypertension, 41.6% had a family history of diabetes, 8.5% had a family history of hyperlipidemia and 24.5% had a family history of heart diseases as in Table 7-5.

Table 7-5: Family History of Diseases among Women

Family History of diseases	Frequency	Percent (%)
Number of women	515	
Family history of blood pressure	209	40.6
Family history of diabetes	214	41.6
Family history of hyperlipidemia	44	8.5
Family history of heart diseases	126	24.5
Blood relationship (consanguinity) between father and mother	224	43.5

7.4.3 Risk Factors for CHD among Women

Table 7-6 shows mean values for the different anthropometric measures and Table 7-7 shows the prevalence of obesity, central and abdominal obesity among women. The women weighed on average 80.6 kg, and had a mean height of 1.56 meters. Their mean BMI (overall obesity) was 33.3 kg/m^2 and 69.2% were obese (BMI $\geq$ 30 kg/m^2). Their mean waist circumference was 98.0 cm. The prevalence of central obesity (WC $\geq$ 88 cm) was 84.2% and the prevalence of abdominal obesity, W/H ratio $\geq$ 0.85 was 51.9%. The majority of the women were obese whether in terms of overall obesity or abdominal adiposity. It has been documented by many studies that overall and abdominal obesity are associated with many non-communicable diseases such as type II diabetes mellitus, cardiovascular and cerebrovascular diseases, digestive disorders, and cancer [275]. Furthermore obesity is a major independent risk factor for the development of hypertension, type II diabetes and dyslipidemia [276]. Please refer to earlier chapters in literature review.

Table7-6: Mean Height, Weight, Hip, Waist, and Thigh Circumferences, BMI, and W/H ratio

Variable Name Mean values of anthropometric measurements	N	Mean (SD)
Standing height, meters	513	1.56 (0.06)
Weight, kg	513	80.6 (15.1)
BMI, kg/m^2	513	33.3 (6.0)
Waist circumference, cm	513	98.0 (12.0)
Thigh circumference, cm	513	119.3 (12.4)
Hip circumference, cm	513	115.5 (11.8)
Waist/hip ratio, cm	513	0.85 (0.06)

Table 7-7: Prevalence of Obesity, Central and Abdominal Obesity among Women, (N=513)

	Frequency	Percentage
Number of women	513	
Overall Obesity (BMI ≥ 30 kg/m^2), %	355	69.2
Central Obesity (WC ≥ 88 cm), %	432	84.2
Abdominal Obesity (W/H ratio ≥ 0.85 cm), %	266	51.9

Tables 7-8 and 7-9 show the prevalence and the mean values for hypertension, diabetes, hyperlipidemia, plasma insulin and the metabolic syndrome among women. The prevalence of hypertension and diabetes was 15.7% and 16.7% respectively without taking into consideration those women who are on medication for being hypertensive or diabetic. 123 out of 157 women, who were diagnosed as having hypertension, were on anti-hypertensive drugs, whereas 83 out of 89 women, who were diagnosed by a physician to have diabetes, were on diabetic medication. Therefore, when anti-hypertensive and diabetic medication was included in the definition of hypertension and diabetes, and using a censored regression model to account for the fact that some women were taking medications for hypertension and diabetes at the time the CHD risk factors were measured, the prevalence of hypertension and diabetes became 42.7% and 22.3% respectively. This censored mean assumes the true value for FBS is that observed or higher for those on medication - for women not on medication, the value for FBS is taken as correct and exact but for those on medication, the value for FBS is taken as at least that observed, since it is assumed that the medication has reduced the FBS level to some extent, but how much is not known. The same applies (later) to blood pressure measurements. The women's lipid profile was as follows: 24.3% had elevated total cholesterol, 31.1% had elevated triglycerides, 49.6% had their HDL-C levels below 1mmol/L, and mean fasting plasma insulin of 9.5 uIU/ml.

Table 7-8: Prevalence of Hypertension, Diabetes, Hyperlipidemia, the Metabolic Syndrome and 10 Years Risk for CHD among Women

	Frequency	Percentage
Number of women	515	
Hypertension SBP ≥ 140/ DBP ≥ 90 mmHg, %	81	15.7
Hypertension SBP ≥ 140/ DBP ≥ 90 mmHg/ medication, %	220	42.7
FBS ≥ 7mmol//L (Diabetic), %	83	16.7
FBS ≥ 7mmol/L (Diabetic) or on medication,%	115	22.3
Elevated Cholesterol > 5.2mmol/L, (200 mg/dl) , %	121	24.3
Elevated Triglycerides ≥ 1.7mmol/L, (150 mg/dl), %	155	31.1
Elevated LDL > 3.5mmol/L, (135 mg/dl), %	99	19.9
Decreased HDL-C < 1mmol/L (40 mg/dl), %	247	49.6
Ratio of T-Chol / HDL-C at high risk > 0.13mmol/L, 5mg/dl	173	34.7
Metabolic syndrome, %	289	58.3
10 years risk for CHD, %*		
Low risk (< 10%)	354	77.5
Medium risk (10-20%)	77	16.8
High risk (>20%)	26	5.7
Total	**457**	**100**

Table 7-9: Mean Values for Serological Measurements

	N	Mean (SD)
Fasting blood glucose, mmol/L	498	6.0 (3.3)
Censoring-adjusted fasting blood sugar, mmol/L	498	6.3 (4.5)
Total Cholesterol, mmol/L	498	4.6 (1.1)
Triglycerides, mg/dl	498	1.6 (1.1)
LDL-C, mmol/L	498	2.8 (1.0)
HDL-C, mmol/L	498	1.1 (0.3)
Ratio of T-Chol / HDL-C	498	0.1 (0.04)
Insulin, uIU/ml	498	9.5 (6.7)

7.5 Life Style Risk Factors

7.5.1 Physical activity

The women tended to lead a sedentary life. When they were asked about whether they practice any kind of physical activity, only 13.4% answered yes. Of these 69 women,

* Calculated from the Framingham risk score

almost half of them walked for almost 3 hours/week. On average, all the women spent 17.4 hours/week watching TV, this being their only connection to the outside world.

7.5.2 Smoking

When women were asked about their smoking habits, 93.4% said they did not smoke. Smoking is more prevalent among younger ages and in men more than women [10].

Table 7-10: Life style risk factors among Women

Variable Name Life style risk factors	Frequency	Percent
Number of women	515	
Physically inactive, %	445	86.6
Smoking habits, %		
Never smoked	481	93.4
Ex-smoker	6	1.2
Current smoker, %	28	5.4
Stress level measurements, %	**Frequency**	**Percent**
Human loss and trauma to study subject	229	44.5
Human loss and trauma to family member	187	36.3
Property loss to subject	5	1
Work related problems	117	22.7
Any of the above stress events	361	70.1

7.5.3 Psychosocial Stress

The women where asked about certain life events during the last six months, such as death of a family member, marital separation, loss of a job, changes in financial conditions, imprisonments, threats, etc. All these questions were grouped into four categories as shown in the second part of Table 7-10. For more information, please see Appendix 2. Seventy percent of the women had been exposed to at least one of the above stress events of psychosocial stressors. Several studies have accumulated giving evidence that life events may be predictive of increased risk of heart diseases [277] [278] [279] [280].

7.6 Principal Characteristics and Parity

This section details the prevalence of CHD risk factors, potential confounders and other covariates by number of children for women in the sample. The number of children

(Parity) has been divided into 5 groups 0, 1-3, 4-6, 7-9 and 10+ to create more stable estimates.

7.6.1 Age and Parity

Table 7-11 shows the distribution of parity among the different age categories of women. Older women had more children in particular parity category 10+ compared to lower age categories. This reflects clearly the drop in fertility rate over time as discussed previously in section 7.1.

Table 7-11: Women's Age and Parity, numbers and percentages by parity

Age groups in years	No. of women	Number of live births					Total %	★P
		0	1-3	4-6	7-9	10+		
< 45	159	19 12.0%	11 6.9%	43 27.0%	59 37.1%	27 17.0%	100%	0.007
45-49	115	11 9.6%	9 7.8%	22 19.1%	39 33.9%	34 29.6%	100%	
50-54	110	6 5.4%	8 7.3%	27 24.6%	35 31.8%	34 30.9%	100%	
55-59	95	5 5.2%	7 7.4%	20 21.0%	22 23.2%	41 43.2%	100%	
60+	35	1 2.8%	3 8.6%	4 11.4%	10 28.6%	17 48.6%	100%	
All ages	514	42 8.2%	38 7.4%	116 22.6%	165 32.0%	153 29.8%	100%	

★ P values for comparison between groups used in this section for all tables are results of χ^2 statistics for categorical variables.

7.6.2 Women's Educational Level and Parity

Do women's educational levels contribute to determining the number of children? As Table 7-12 and Figure 7.1 indicate women with no formal education tended to be the highest among those of parity 10+. In contrast, the proportion of women with university education fell across the parity groups, where no women with parity 10+ had university or college education at all compared to the other parity groups. Parity groups 1-3 and 4-6 seemed to have the highest university levels of or college education. This is consistent with the effect of education being to lead women to tend to reduce the size of their families and bear fewer children; however education did not lead to women having no children, as this is not the norm in Palestinian culture.

Figure 7-1: Women's Education Level; percentage of women at each level by Parity

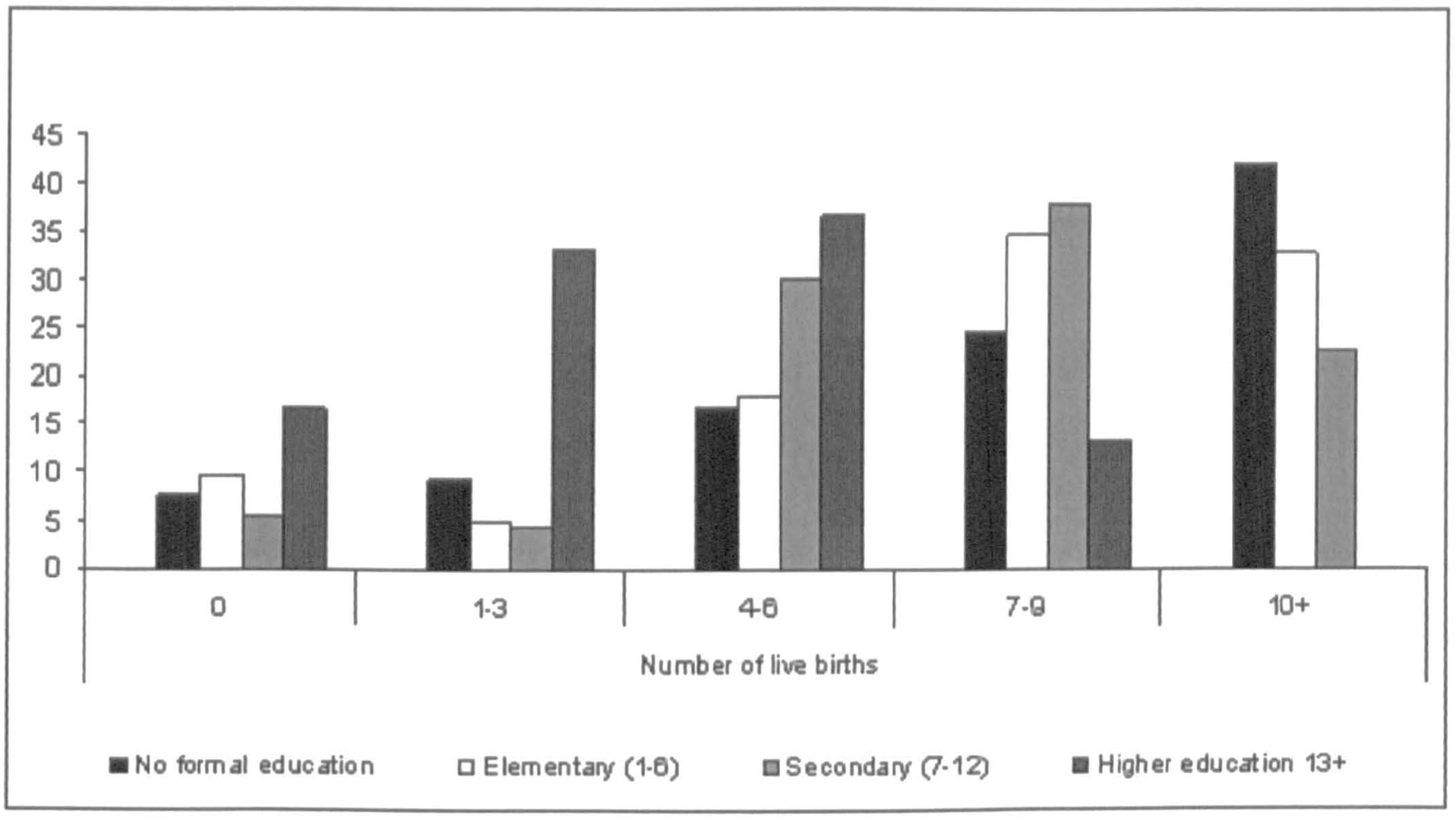


Table 7-12: Women's Educational Level and Parity

Education level	No. of women	Number of live births					Total %	★P
		0	1-3	4-6	7-9	10+		
No formal education	119	9 7.6%	11 9.2%	20 16.8%	29 24.4%	50 42.0%	100%	<0.0001
Elementary (1-6)	199	19 9.6%	10 5.0%	36 18.1%	69 34.7%	65 32.7%	100%	
Secondary (7-12)	167	9 5.4%	7 4.2%	50 29.9%	63 37.7%	38 22.8%	100%	
Higher education 13+	30	5 16.7%	10 33.3%	11 36.7%	4 13.3%	0 0.0%	100%	
Total	515	42 8.2%	38 7.4%	117 22.7%	165 32.0%	153 29.7%	100%	

7.6.3 Women's Employment and Parity

The majority of women did not work. The percentage of employed women decreased with increasing parity as seen in Table 7-13. (In this and later tables, the percentages are given by parity groups, since working status etc may be influenced by parity; in the previous tables, parity was more likely to be a consequence of age and education.) The higher the parity, the less likely it was for women to work and around 9% of women in the 10+ parity group were working compared 26% and 34% among parity 0 and parity

1-3 respectively. Women with many children will have less time to seek a job as they most probably will be busy looking after a large family, compared to women with smaller family sizes. One should bear in mind that women of higher parity tended to be older, less educated and therefore their chances of getting a job were less; parity may be a consequence of these adverse factors as well as a contribution to non-employment. In addition, these women appeared most probably to be seeking employment through private business ventures, as shown in Table 7-13. One notes that private businesses allow them to stay at home and at the same time contribute to their family income.

There were women in all parity groups except the nulliparous who worked as unskilled workers. Employed women were more frequently found among the lowest parity groups, 0, 1-3 and 4-6, and being in skilled jobs was more frequent in these parity groups also. Moreover, women in the parity 10+ group worked mostly as unskilled labourers and in private business.

Table 7-13: Women's Employment and Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Currently employed, %						<0.0001
Number of women	42	38	117	165	153	
No and Percent not employed	31 73.8%	25 65.8%	94 80.3%	147 89.1%	139 90.9%	
No and Percent employed	13 26.2%	13 34.2%	23 19.7%	18 10.9%	14 9.1%	
Total	100%	100%	100%	100%	100%	
Occupation, % *						0.013
Number of women	11	13	23	18	14	
No and Percent Unskilled worker	0 0.0%	3 23.1%	6 26.1%	4 22.2%	3 21.5%	
No and Percent Skilled worker	3 27.3%	3 23.1%	5 21.7%	2 11.1%	1 7.1%	
No and Percent Employee: clerical & professional	6 54.6%	6 46.1%	8 34.8%	4 22.3%	0 0.0%	
No and Percent Private business	2 18.2%	1 7.7%	4 17.4%	8 44.4%	10 71.4%	
Total	100%	100%	100%	100%	100%	

* Percentages of those in employment.

7.6.4 Husband's Educational Level and Employment with Parity

The total number of schooling years completed by the husbands was used as a proxy indicator of longer term socio-economic status (SES). The husband's schooling years was inversely associated with parity as shown in Table 7-14: the higher the parity the less educated the husband was. Parity 10+ and parity 0 has the highest percentages of husbands with no formal education amounting to 21% for parity 10+ and 45% for parity 0. In addition, parity 10+ had the least percentages of husbands completing college or university education.

On the other hand, the husband's employment for women who have ever been married tended to increase with increasing parity. It is important to note that husbands seldom owned any private business, instead their occupation varied from unskilled workers to employees and working in international organizations. The lack of focus on private business by husbands can be an indicator of women's participation in supporting their families through the establishment of their own private businesses, which has been mentioned in the sections above

Table 7-14: Husband's Educational Level and Employment with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Husband's education,%						<0.0001
Number of women	20	36	112	162	149	
No and Percent No formal education	9 45.0%	8 22.2%	14 12.5%	22 13.6%	32 21.5%	
No and Percent Elementary (1-6)	8 40.0%	13 36.1%	30 26.8%	53 32.7%	62 41.6%	
No and Percent Secondary (7-12)	1 5.0%	8 22.2%	46 41.1%	68 42.0%	47 31.5%	
No and Percent Higher education (13+)	2 10.0%	7 19.4%	22 19.6%	19 11.7%	8 5.4%	
Total	100%	100%	100%	100%	100%	
Husband currently employed, %						<0.0001
Number of women	21	38	117	165	153	
No and Percent husband employed	5 23.8%	12 31.6%	59 50.4%	93 56.4%	72 47.1%	
No and Percent husband not employed	6 28.6%	9 23.7%	22 18.8%	44 26.7%	60 39.2%	
No and Percent not applicable (divorced, separated and widowed women where there is no husband)	10 47.6%	17 44.7%	36 30.8%	28 17.0%	21 13.7%	
Total	100%	100%	100%	100%	100%	
Husband's Occupation %						0.108
Number of women	5	12	59	93	72	
No and Percent Unskilled worker	2 40.0%	3 25.0%	9 15.25%	30 32.3%	31 43.1%	
No and Percent Skilled worker	0 0.0%	0 0.0%	7 11.9%	18 19.4%	11 15.3%	
No and Percent Employee	1 20.0%	5 41.7%	20 33.9%	18 19.4%	12 16.7%	
No and Percent International organization	2 40.0%	4 33.3%	23 39.0%	26 28.0%	18 25.0%	
No and Percent Private business	0 0.0%	0 0.0%	0 0.0%	1 1.1%	0 0.0%	
Total	100%	100%	100%	100%	100%	

7.6.5 Marital Status with Parity

Table 7-15 shows marital status by parity groups. The majority of women, except among the nulliparous were married and only 21 were single – all nullipars. Being married was more frequent among those of higher parity. Women in parity groups 1-3 and 4-6 had the highest percentage of being widowed: 23.8% and 21.4% compared to the other parity groups. Also parity 1-3 had the highest percentage of being separated or divorced compared to the other parity grouping. If husbands were alive, or present, the number of children would have definitely increased.

Table 7-15: Marital Status with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Marital status,%						<0.0001
Number of women	42	38	117	165	153	
No and Percentage married	11 26.2%	21 55.3%	81 69.2%	137 83.0%	132 86.3%	
No and Percentage single	21 50.0%	0 0.0%	0 0.0%	0 0.0%	0 0.0%	
No and Percentage divorced	4 9.5%	5 13.2%	6 5.1%	2 1.2%	0 0.0%	
No and Percentage separated	0 0.0%	3 7.9%	5 4.3%	1 0.6%	2 1.3%	
No and Percentage widowed	6 14.3%	9 23.7%	25 21.4%	25 15.2%	19 12.4%	
Total	100%	100%	100%	100%	100%	

7.6.6 Family Affluence Scale with Parity

The women in the 10+ parity group were relatively poor compared to the other parity groups as shown in Table 7-16. Wealth status decreased with increasing parity and the percentage of women with the lower parity groups 0 and 1-3 were better off at 54.7% and 50.0% respectively, compared to women in the higher parity groups.

Table 7-16: Family Affluence Scale with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Family affluence scale, %						<0.0001
Number of women	42	38	117	165	153	
No and Percentage Poor	13 31.0%	7 18.4%	40 34.2%	81 49.1%	84 54.9%	
No and Percentage Average	6 14.3%	12 31.6%	39 33.3%	61 37.0%	46 30.1%	
No and Percentage Better off	23 54.7%	19 50.0%	38 32.5%	23 13.9%	23 15.0%	
Total	100%	100%	100%	100%	100%	

7.6.7 Physical Activity

Physical activity decreased with increasing parity. Women among the 1-3 and 0 parity groups had the highest percentage of being relatively physically active, 23.7% and 19.0% respectively compared to the other parity groups, 4-6, 7-9 and 10+, where the percentages were 16.2%, 11.5% and 9.2% respectively as shown in Table 7-17. These trends, however, were of much less statistical significance

Table 7-17: Physical Activity with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Physical activity,%						
Number of women	42	38	117	165	152	
No and Percentage Active	34 19.0%	29 23.7%	98 16.2%	146 11.5%	138 9.2%	
No and Percentage Inactive	8 81.0%	9 76.3%	19 83.8%	19 88.5%	14 90.8%	0.084
Total	100%	100%	100%	100%	100%	

7.6.8 Household Crowded Scale

Living in crowded houses, which accommodates more than 2 persons per room, increased with increasing parity where it reached 55.5% among parity 10+ group compared to 21.6% among parity 1-3 and 31.0% among parity 0 as shown in Table 7-18.

Table 7-18: Household Crowded Scale with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Crowdedness persons / room, %						<0.001
Number of women	42	37	116	163	153	
No and Percentage not Crowded ≤ 1	23 54.7%	15 40.5%	28 24.1%	17 10.4%	20 13.1%	
No and Percentage Moderate >1& ≤ 2	6 14.3%	14 37.9%	47 40.5%	62 38.0%	48 31.4%	
No and Percentage Crowded > 2	13 31.0%	8 21.6%	41 35.4%	84 51.6%	85 55.5%	
Total	100%	100%	100%	100%	100%	

7.6.9 Smoking Status

The majority of women did not smoke and the trend with parity was far from statistically significant. Women with parity 10+ were most likely to be the highest passive smokers as they spent most of their time at home.

Table 7-19: Smoking Status with parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Smoking status, %						0.395
Number of women	42	38	117	165	153	
No and Percentage never smoked	39 92.8%	36 94.7%	105 89.7%	153 92.7%	148 96.7%	
No and Percentage current smoker	2 4.8%	2 5.3%	11 9.4%	10 6.1%	3 2.0%	
No and Percentage ex-smoker	1 2.4%	0 0.0%	1 0.9%	2 1.2%	2 1.3%	
Total	100%	100%	100%	100%	100%	
Passive smoker, %						0.004
Number of women	42	38	117	165	153	
No and Percentage said Yes	18 42.9%	20 52.6%	69 59.0%	118 71.5%	101 66.0%	
No and Percentage said No	24 57.1%	18 47.4%	48 41.0%	47 28.5%	52 34.0%	
Total	100%	100%	100%	100%	100%	

7.6.10 Stress Status

Table 7-20 shows the distribution of stress status with parity groups. Apart from parity 0, stress from all events among the study population increased significantly with increasing parity where it reached 73.3% and 78.4% among parity 7-9 and parity 10+ groups respectively.

Table 7-20: Stress Status with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Stress status: any one of the stress events						<0.0001
Number of women	42	38	117	165	153	
Number and Percentage said Yes to one or more	22 52.4%	18 47.4%	80 68.4%	121 73.3%	120 78.4%	
Number and Percentage said No to all	20 47.6%	20 52.6%	37 31.6%	44 26.7%	33 21.6%	
Total	100%	100%	100%	100%	100%	

7.6.11 History of Infertility

History of infertility was defined as "if a woman ever tried for one straight year or more to become pregnant and during that time did not become pregnant". History of infertility was high among the parity 0 group compared to other parity groups. Fifteen out of the 21 married women stated they were infertile. Infertility is negatively regarded in Palestinian society and places women under considerable stress whether from their husbands, their families or society at large. Infertile women normally end up being divorced or separated where the husband will marry another that supposedly can bear many children to maintain the name and wealth of the family.

Table 7-21: History of Infertility with Parity excluding single women

Risk factor	Number of live births					★P *
	0	1-3	4-6	7-9	10+	
History of Infertility, %						
Number of women	21	38	117	165	153	
No and Percentage said Yes	15 71.4%	7 18.4%	11 9.4%	8 4.8%	12 7.8%	
No and Percentage said No	6 28.6%	31 81.6%	106 90.6%	157 95.2%	141 92.2%	<0.0001
Total	100%	100%	100%	100%	100%	

* P-value for ever-married women. Excluding nulliparous women, p= 0.044

When the analysis of history of infertility was repeated excluding nulliparous women, the history of infertility gave same results except for p value. As shown in the footnote to Table 7-21.

7.6.12 Ever Used Oral Contraceptive Pill and Menopausal Status

Table 7-22 shows percentages of women who reported they had ever used the oral contraceptive pill and menopausal status. Apart from parity 0, the percentage of women in the different parity groups who reported ever use of contraceptive pills increased with increasing parity. On the other hand, menopausal status increased with increasing parity. Women with many children seem to have gone into menopausal status before those with less parity. The women with high parity were older and the non-menopausal women younger, yet all women participated in the study had finished their childbearing. The changes in contraceptive use may be more associated with behavioural differences between the generations.

Table 7-22: Ever Used Oral Contraceptive Pill, Menopausal Status and Parity

Risk factor	Number of live births					★P*
	0	1-3	4-6	7-9	10+	
Ever used oral contraceptive %						
Number of women	42	38	117	164	153	
No and Percentage never used	38 90.5%	29 76.3%	69 59.0%	89 54.3%	81 52.9%	
No and Percentage ever used	4 9.5%	9 23.7%	48 41.0%	75 45.7%	72 47.1%	<0.0001
Total	100%	100%	100%	100%	100%	
Menopausal status, %						
Number of women	41	38	117	165	153	
No and Percent not menopausal	30 73.2%	18 47.4%	66 56.4%	97 58.8%	74 48.4%	
No and Percent menopausal	11 26.8%	20 52.6%	51 43.6%	68 41.2%	79 51.6%	0.039
Total	100%	100%	100%	100%	100%	

* P-value for ever-married women

7.6.13 Type II Diabetes Mellitus

Diabetes (measured as raised fasting blood sugar or using medication) increased with parity. Apart from parity 0, diabetes prevalence increased across parity categories starting from parity 1-3 group onward ranging from 15.8 % to 25.5 %. The prevalence of diabetes among nulliparous women was 21.4%. This may imply a J-shaped relationship between diabetes with parity; however the differences were not statistically significant, as shown in Table 7-23. The increasing trend excluding parity zero is also not significant. In section 7.7, it is, however, shown that there was a significant increase in mean fasting blood sugar with parity.

Table 7-23: Type II Diabetes Mellitus with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Diabetic ≥7mmol/L or on medication, %						
Number of women	42	38	117	165	153	
No and Percentage normal	33 78.6%	32 84.2%	92 78.6%	129 78.2%	114 74.5%	0.749
No and Percentage diabetic	9 21.4%	6 15.8%	25 21.4%	36 21.8%	39 25.5%	
Total	100%	100%	100%	100%	100%	

7.6.14 Hypertension

Hypertension varied rather less among the different parity groups, although mean SBP and DBP showed significant increases with increasing parity. (Mean values are not shown in this table, but are in Section 7.7 and Table 7-28)

Table 7-24: Hypertension with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Hypertension SBP ≥ 140 mmHg / DBP ≥ 90 mmHg/ medication, %						
Number of women	42	38	117	165	153	
No and Percentage normal	29 69.1%	24 63.2%	68 58.1%	93 56.4%	81 52.9%	0.382
No and Percentage hypertensive	13 30.9%	14 36.8%	49 41.9%	72 43.6%	72 47.1%	
Total	100%	100%	100%	100%	100%	

7.6.15 Overall Obesity

Table 7-25 shows overall obesity with parity in groups. BMI ≥ 30 is increasing with increasing parity, except for parity 4-6 where it showed a decline compared to the other parity groups.

Table 7-25: Overall obesity with parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
BMI, %						
Number of women	42	38	116	164	153	
No and Percentage Non-obese	19 45.2%	14 36.2%	52 44.8%	40 24.4%	33 21.6%	<0.0001
No and Percentage Obese	23 54.8%	24 63.2%	64 55.2%	124 75.6%	120 78.4%	
Total	100%	100%	100%	100%	100%	

7.6.16 Central and Abdominal Obesity

Apart from parity 0, waist circumference increased significantly with increasing parity. The higher level for zero parity might imply a J-shaped relationship. On the other hand,

abdominal obesity did not show a significant association with parity as shown in Table 7-26.

Table 7-26: Central and abdominal obesity with parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Central obesity, %						
Waist circumference ≥ 88 cm						
Number of women	42	38	116	164	153	
No	11 26.2%	12 31.6%	27 23.3%	19 11.6%	12 7.8%	
Yes	31 73.8%	26 68.4%	89 76.7%	145 88.4%	141 92.2%	<0.0001
Total	100%	100%	100%	100%	100%	
Abdominal obesity,						
W/H ratio ≥ 0.85 cm						
Number of women	42	38	116	164	153	
No	17 40.5%	22 57.9%	58 50.0%	83 50.6%	67 44.8%	
Yes	25 59.5%	16 42.1%	58 50.0%	81 49.4%	86 56.2%	0.385
Total	100%	100%	100%	100%	100%	

7.6.17 The Metabolic Syndrome and 10-years risk

The association between parity and the Metabolic Syndrome, which is defined according to the International Diabetic Federation as the clustering of the most dangerous heart attack risk factors: diabetes and pre-diabetes, abdominal obesity, high cholesterol and high blood pressure, tended to show a U-shaped relationship; p= 0.003, with a drop at parity 1-3 children. Also the metabolic syndrome increased with increasing parity as shown in Table 7-27. 10-years risk for CHD, on the other had did not show changes with overall statistical significance.

Table 7-27: The Metabolic Syndrome and 10 Years Risk for CHD with Parity

Risk factor	Number of live births					★P
	0	1-3	4-6	7-9	10+	
Metabolic Syndrome (MS), %						
Number of women	40	33	110	160	153	
No and Percentage without MS	19 47.5%	22 66.7%	48 43.6%	70 43.8%	48 31.4%	
No and Percentage with MS	21 52.5%	11 33.3%	62 56.4%	90 56.3%	105 68.6%	0.003
Total	100%	100%	100%	100%	100%	

10 years Risk For CHD, %						
Number of women	40	33	109	161	153	
No and Percentage, low risk	32 86.5%	26 86.7%	81 77.9%	122 79.7%	93 69.9%	0.199
No and Percentage, medium risk	4 10.8%	4 13.3%	19 18.3%	23 15.0%	27 20.3%	
No and Percentage, high risk	1 2.7%	0 0.0%	4 3.8%	8 5.3%	13 9.8%	
Total	100%	100%	100%	100%	100%	

7.7 Parity and Coronary Heart Disease Risk Factors Shown as Mean Values

This section details the association of those CHD risk factors which can be expressed as mean values and covariates with parity in groups. The following table shows the means (SD) values for these risk factors, other covariates and potential confounders by number of children among women aged 40-65 years.

Table 7-28: Means (SD) of CHD risk factors, potential confounders and other covariates by number of children among women aged 40-65 years

Risk Factor	Number of Live Births					★P
	0	1-3	4-6	7-9	10+	
Number of women	42	38	116	164	153	
Age	47.0 (6.23)	49.5 (6.6)	48.4 (6.1)	48.5 (6.3)	51.7 (6.2)	<0.001
Reproductive history						
Age at 1st marriage	26.0 (9.6)	23.4 (6.6)	20.0 (4.1)	18.1 (3.0)	16.5 (2.3)	<0.001
Age at 1st pregnancy	29.4 (9.7)	25.3 (6.4)	20.9 (4.2)	18.7 (2.9)	17.2 (2.2)	<0.001
Age at 1st birth		26.0 (6.4)	21.7 (4.2)	19.4 (2.9)	18.0 (2.2)	<0.001
Age at last birth		30.9 (7.7)	33.5 (4.9)	35.5 (3.9)	38.2 (3.8)	<0.001
Years between 1st and last birth		4.8 (3.9)	11.9 (4.9)	16.0 (3.6)	20.2 (3.9)	<0.001
Years since last birth		18.5 (10.2)	14.9 (7.5)	12.9 (6.7)	13.5 (6.8)	<0.001
Miscarriage/ abortion	2.3 (1.3)	2.3 (2.9)	2.3 (1.9)	2.3 (1.9)	2.6 (1.7)	0.801
Stillbirths		1.0 (0.0)	1.4 (0.7)	1.4 (0.7)	1.2 (0.4)	0.560
Age at menarche	13.3 (1.4)	13.3 (1.4)	13.3 (1.4)	13.4 (1.4)	13.4 (1.4)	0.958
Age at menopause	46.5 (6.7)	45.7 (7.7)	47.4 (6.1)	48.3 (4.9)	49.5 (4.3)	0.029
CHD risk factors						
Censored Systolic BP, mmHg	126.4 (3.2)	129.7 (4.5)	133.1 (2.6)	135.9 (2.1)	139.9 (2.7)	<0.0001
Censored DBP, mmHg	80.7 (1.9)	84.1 (2.4)	83.5 (1.4)	84.9 (1.0)	84.9 (1.1)	<0.0001
Censored Fasting Blood Sugar, mmol/L	5.7 (0.4)	4.9 (0.3)	6.0 (0.3)	6.5 (0.3)	6.7 (0.3)	<0.0001
Cholesterol, mmol/L	4.4 (1.1)	4.7 (1.3)	4.6 (1.0)	4.5 (1.0)	4.7 (1.2)	0.411

Risk Factor	Number of Live Births					★P
	0	1-3	4-6	7-9	10+	
Triglycerides, mmol/L	1.35 (0.6)	1.33 (1.2)	1.51 (1.0)	1.55 (1.0)	1.75 (1.3)	0.080
HDL-C, mmol/L	1.10 (0.3)	1.14 (0.3)	1.08 (0.3)	1.06 (0.3)	1.04 (0.3)	0.378
LDL-C, mmol/L	2.5 (1.0)	2.6 (1.1)	2.8 (1.0)	2.7 (1.0)	2.9 (1.1)	0.225
Chol/HDL-C ratio, mmol/L	0.11 (0.03)	0.11 (0.5)	1.2 (0.04)	0.12 (0.05)	0.12 (0.04)	0.242
Insulin uIU/ml	8.4 (4.6)	10.7 (8.8)	9.3 (6.2)	10.2 (8.2)	8.9 (5.2)	0.305
Anthropometric Risk factors						
Height, m	1.6 (0.01)	1.6 (0.08)	1.6 (0.06)	1.6 (0.07)	1.6 (0.06)	0.385
Weight, kg	76.4 (13.9)	79.3 (22.8)	77.2 (14.6)	82.3 (14.1)	82.6 (14.0)	0.006
BMI, kg/m^2	31.9 (6.5)	32.7 (7.3)	31.6 (5.6)	33.8 (5.5)	34.5 (5.9)	0.001
Waist circumference, cm	94.5 (11.3)	95.8 (14.7)	95.1 (12.8)	98.7 (11.5)	101.1 (10.5)	<0.001
Thigh circum, cm	114.6 (12.7)	118.4 (16.1)	116.3 (11.1)	120.9 (11.3)	121.4 (12.5)	<0.001
Hip circum, cm	110.3 (12.3)	114.9 (15.4)	112.6 (10.8)	117.0 (10.5)	117.7 (11.9)	<0.001
W/H ratio, cm	0.86 (0.04)	0.83 (0.06)	0.84 (0.07)	0.86 (0.06)	0.85 (0.06)	0.066
Other Covariates						
Years of schooling	6.0 (4.7)	7.1 (6.2)	6.8 (4.4)	5.8 (3.7)	4.1 (3.4)	<0.001
Husband's years of education	3.6 (4.6)	6.8 (5.4)	8.3 (5.0)	7.4 (4.4)	5.6 (4.1)	<0.001
Rooms/ household	2.8 (1.3)	3.6 (1.3)	3.5 (1.2)	3.8 (1.1)	3.9 (1.0)	<0.001
Hours/week practice physical activity	1.8 (1.4)	3.9 (4.3)	3.4 (2.5)	2.6 (2.5)	3.8 (2.7)	0.356
Hours/week watch TV	19.0 (12.4)	16.6 (10.3)	17.9 (11.5)	16.6 (11.8)	17.6 (13.5)	0.786
CHD Risk Score						
10-years CHD risk score	0.05 (0.05)	0.05 (0.04)	0.07 (0.06)	0.07 (0.07)	0.09 (0.08)	0.0004
Log 10-years CHD risk score	-3.6 (1.14)	-3.5 (0.93)	-3.2 (1.0)	-3.2 (1.1)	-2.9 (1.1)	0.0004

★P values for comparison between groups are results of a one way analysis (ANOVA) for continuous variables.

Continuous variables are mean ±SD

Women with higher parity tended to have married at an early age and accordingly to have had an early age of first pregnancy and age at first birth compared with women of lower parity and nulliparous women as shown in Table 7-28.

Higher parity women tended to be older and parity increases with increasing age, (see also Table 7-11). Those women in the sample who were older tended to have had more children than younger women in spite of the fact that all women participating in the study had finished their child bearing. This reflects the fall in total fertility among women over the past years.

Mean Systolic Blood Pressure increased significantly with increasing parity. Women with parity 10+ children had higher mean systolic blood pressures compared to parity 0 and parity 1-3, and accordingly there were a greater percentage of higher parity women with hypertension.

Mean Fasting Blood Sugar tended to increase with increasing parity except for parity 0 where it was higher than parity 1-3, which might imply a J-shaped relationship. Mean FBS was lower among parity 1-3. The association between mean fasting blood sugar and parity in groups was also statistically significant as shown in Table 7-28.

Triglycerides tended to increase with increasing parity except for parity 0 where it was more elevated than parity 1-3 group. Starting from parity 1-3, mean HDL-C levels decreased slightly with increasing parity. However, it is worth mentioning that the association between parity and all the lipid profile risk factors was not statistically significant.

Women in all parity groups tended to be obese with more than half with a BMI ≥ 30 kg/m^2 (Table 7-28); mean BMI increased significantly with increasing parity. The same applies to waist circumference among the different parity groups, where it increased with increasing parity. The trend in W/H ratio was much less strong and did not seem to be significant. The W/H ratio was higher among the parity 0 group and was similar to the higher parity groups 7-9 and 10+, though the lack of statistical significance should be noted.

There was a significant association between increased parity and educational level. Women in the lower parity groups tended to have higher levels of education compared to the higher parity groups. Husband's years of schooling which is a longer term proxy

indicator of the SES of the family, showed more or less the same pattern as women's education. Husband's education decreased with increasing parity except for parity 0 group where the husband's had the least years of education.

Chapter 8
PARITY AND ANTHROPOMETRIC MEASUREMENTS

The presentation of results is now focused on particular risk factors for coronary heart disease (CHD), starting with those based on anthropometric measures. Chapter 8 is divided into four sections. Section 8.1 discusses characteristics associated with obesity, central and abdominal adiposity. Section 8.2 discusses obesity with parity. Section 8.3 discusses parity with central obesity and section 8.4 discusses parity with abdominal obesity.

Several anthropometric measurements were used in assessing the association between parity and obesity as they represent different aspects of body fat distribution and therefore relate differently to health outcomes [270]. BMI was used to assess overall obesity, waist circumference was used to assess central obesity, and W/H ratio was used to assess abdominal obesity. Hence, in this chapter, we investigated each of these obesity indices risk factors in relation to parity.

As has been stated above, the mean BMI was 33.3 kg/m^2 and 69.2% of women were obese (BMI $\geq$ 30 kg/m^2). The women's mean waist circumference was 98 cm and the prevalence of central obesity (WC $\geq$ 88 cm) was 84.2%. Their mean waist to hip ratio was 0.85 cm and 51.9% of women were having abdominal obesity (W/H ratio $\geq$ 0.85 cm), (see sections 7.4.3 Risk Factors for CHD in Women). Table 8-1 shows these characteristics associated with obesity, central and abdominal obesity in relation to other variables.

Obese women tended to be older, married or widowed, had more pregnancies and children, and were less likely to be educated, more often unemployed, and less physically active. They tended to have more assistance at home from their daughters or daughters-in-laws, which encourages a sedentary life style. Obese women tended to have decreased HDL-C levels, elevated triglycerides, elevated diastolic, systolic blood pressure and hypertension.

Women with central obesity shared many of the characteristics that obese women had. They tended to be older and of menopausal status, living with their husbands and or widowed. They got married at an early age and had an early age at first birth and therefore had more gravidity and parity. Women with central obesity were less likely to be educated, more often unemployed, spending more hours watching TV, and getting

household assistance and therefore tended to be physically inactive. Women with central obesity reported having more polycystic ovary syndrome, having elevated metabolic risk factors and a decreased HDL-C level, elevated SBP, DBP, and hypertension, and elevated fasting blood sugar.

Women with abdominal obesity tended to be older and more frequently menopausal, married and / or widowed, use more oral contraceptive pills, and have elevated triglycerides, DSP, SBP and elevated fasting blood sugar. Women with abdominal obesity tended to have decreased HDL-C and less education.

When women were asked about how they perceive their weight and their self rating of obesity, 19.1% of women who had BMI $\geq$ 30kg/m^2 rated themselves as being underweight and 33.3% of women with central adiposity WC $\geq$ 88 cm rated themselves as being underweight.

Table 8-1: Characteristics associated with potential risk factors
BMI $\geq$ 30kg/m2, WC $\geq$ 88 cm & W/H ratio $\geq$ 0.85 cm

Characteristic	Number of women	Obese BMI $\geq$ 30kg/m^2 n %	P value	WC $\geq$ 88 cm, % n %	P-value	W/H ratio $\geq$ 0.85 cm, % n %	P value
Demographic and socio-economic variables							
Age			0.069		**<0.0001**		**<0.0001**
<45	158	(98) 62.0		(117) 74.1		(64) 40.5	
45-49	115	(85) 73.9		(97) 84.4		(57) 49.6	
50.54	109	(74) 67.9		(95) 87.2		(63) 57.8	
55-59	95	(69) 72.6		(90) 94.7		(55) 57.9	
60+	35	(29) 82.9		(33) 94.3		(27) 77.1	
Women's education, %			**0.015**		**<0.0001**		**0.004**
No formal education	119	(78) 73.1		(111) 93.3		(77) 64.7	
Elementary	198	(140) 70.7		(168) 84.9		(96) 48.5	
Secondary	166	(115) 69.3		(137) 82.5		(83) 50.0	
Higher education	30	(13) 43.3		(16) 53.3		(10) 33.3	
Marital status			0.074		**0.004**		**0.028**
Married	382	(265) 69.4		(325) 85.1		(186) 48.7	
Single	21	(11) 52.4		(14) 66.7		(14) 66.7	
Divorced/ separated	28	(16) 57.1		(19) 67.9		(13) 46.4	
Widowed	82	(63) 76.8		(74) 90.5		(53) 64.6	
Currently employed			**0.022**		**0.001**		0.352
No	434	(309) 71.2		(375) 86.4		(229) 52.8	
Yes	79	(46) 58.2		(57) 72.2		(73) 46.8	

Characteristic	Number of women	Obese BMI ≥ 30kg/m^2 n %	P value	WC ≥ 88 cm, % n %	P-value	W/H ratio ≥ 0.85 cm, % n %	P value
Occupation			0.478		0.163		0.400
Unskilled worker	16	(11) 68.8		(13) 81.3		(9) 56.3	
Skilled worker	14	(9) 64.3		(9) 64.3		(5) 35.7	
Employee	24	(11) 45.8		(14) 58.3		(9) 37.5	
Private business	25	(15) 60.0		(21) 84.0		(14) 56.0	
Husband's education			**0.002**		**0.001**		0.056
No formal education	85	(53) 62.4		(76) 89.4		(47) 55.3	
Elementary	165	(130) 78.8		(150) 91.9		(91) 55.1	
Secondary	170	(120) 70.6		(139) 81.8		(86) 50.6	
Higher education	57	(31) 54.4		(40) 70.2		(20) 35.1	
Husband currently employed			0.717		0.660		0.059
Yes	241	(170) 70.5		(202) 83.8		(112) 46.5	
No	141	(95) 67.4		(123) 87.2		(74) 52.5	
Not applicable	110	(79) 71.8		(93) 84.6		(66) 60.0	
Own automatic washing machine			**0.004**		**0.004**		0.577
No	398	(298) 72.4		(345) 86.7		(209) 52.5	
Yes	115	(67) 58.3		(87) 75.7		(57) 49.6	
Family affluence scale			0.068		0.075		0.788
Poor	223	(158) 70.9		(186) 83.4		(118) 52.9	
Average	164	(120) 73.2		(146) 89.0		(86) 52.4	
Better off	126	(77) 61.1		(100) 79.4		(62) 49.2	
Behavioural Risk Factors							
Physical activity			**<0.0001**		0.071		0.139
No	443	(320) 72.3		(378) 85.3		(235) 53.1	
Yes	69	(34) 49.3		(53) 76.8		(30) 43.5	
Smoking habits			0.180		0.699		0.642
Never smoked	479	(336) 70.2		(405) 84.6		(250) 52.2	
Ex-smoker	6	(4) 66.7		(5) 83.3		(2) 33.3	
Current smoker	28	(15) 53.6		(22) 78.6		(14) 50.0	
Watch TV			0.166		0.336		0.278
No	31	(18) 58.1		(28) 90.3		(19) 61.3	
Yes	482	(337) 69.9		(404) 83.8		(247) 51.2	

Characteristic	Number of women	Obese BMI ≥ 30kg/m^2 n %	P value	WC ≥ 88 cm, % n %	P-value	W/H ratio ≥ 0.85 cm, % n %	P value
Hours/week watch TV			0.393		**0.009**		0.430
≤ 4	24	(18) 75.0		(23) 95.8		(15) 62.5	
5-10	149	(97) 65.1		(114) 76.5		(72) 48.3	
11-20	132	(92) 69.7		(110) 83.3		(64) 48.5	
21+	177	(130) 73.5		(157) 88.7		(96) 54.2	
Assistance in house-work			**<0.0001**		**<0.0001**		0.242
No	141	(75) 53.2		(101) 71.6		(66) 46.8	
Yes	371	(279) 75.2		(330) 89.0		(199) 53.6	
Stress level			0.219		0.309		0.949
All events combined (1-16)							
No	153	(100) 65.4		(125) 81.7		(79) 51.6	
Yes	360	(255) 70.8		(307) 85.3		(187) 51.9	
Reproductive Health Factors							
Parity			**<0.0001**		**<0.0001**		0.385
0	42	(23) 54.8		(31) 73.8		(25) 59.5	
1-3	38	(24) 63.2		(26) 68.4		(16) 42.1	
4-6	116	(64) 55.2		(89) 76.7		(58) 50.0	
7-9	164	(124) 75.6		(145) 88.4		(81) 49.4	
10+	153	(120) 78.4		(141) 92.2		(86) 56.2	
Age at 1st marriage,			0.492		0.050		0.227
<18	231	(165) 71.4		(204) 88.3		(125) 54.1	
18+	261	(179) 68.6		(214) 82.0		(127) 48.7	
Age at 1st birth			0.093		**0.004**		0.266
≤ 18	172	(129) 75.0		(157) 91.3		(94) 54.7	
> 18	300	(203) 67.7		(244) 81.3		(148) 49.3	
Gravidity 5			**0.005**		**0.002**		0.837
0	38	(21) 55.3		(28) 73.7		(21) 55.3	
1- 3	33	(22) 66.7		(24) 72.7		(16) 48.5	
4- 6	65	(36) 55.4		(48) 73.8		(30) 46.2	
7- 9	135	(92) 68.2		(116) 86.0		(73) 54.1	
10+	242	(184) 76.0		(216) 89.3		(126) 52.1	
Age at menarche			0.071		0.554		0.160
≤ 11	39	(31) 79.5		(34) 87.2		(17) 43.6	
12	106	(81) 76.4		(93) 87.7		(64) 60.4	
13	138	(95) 68.8		(111) 80.4		(63) 45.7	
14	133	(88) 66.2		(110) 82.7		(72) 54.1	
15+	90	(54) 60.0		(77) 85.6		(46) 51.1	
History of infertility			0.765		0.423		0.739
No	439	(306) 69.7		(371) 84.5		(226) 51.5	
Yes	53	(38) 71.7		(47) 88.7		(26) 49.1	

Characteristic	Number of women	Obese BMI ≥ 30kg/m^2 n %	P value	WC ≥ 88 cm, % n %	P-value	W/H ratio ≥ 0.85 cm, % n %	P value
Pregnancy ended as abortion or miscarriage			0.230		0.222		0.759
No	164	(121) 73.8		(144) 87.8		(83) 50.6	
Yes	311	(213) 68.5		(260) 83.6		(162) 52.1	
Pregnancy ended as a stillbirth			0.066		0.077		0.144
No	410	(282) 68.8		(344) 83.9		(206) 50.3	
Yes	65	(52) 80.0		(60) 92.3		(39) 60.0	
Have you ever had polycystic ovaries			0.057		0.004		0.456
No	493	(346) 70.2		(421) 65.4		(255) 51.7	
Yes	13	(6) 46.2		(8) 61.5		(8) 61.5	
Ever used OC			0.410		0.710		**0.004**
No	304	(215) 70.7		(258) 84.9		(174) 57.2	
Yes	208	(140) 67.3		(174) 83.7		(92) 44.2	
Have your periods stopped now			0.108		**0.001**		**<0.0001**
No	284	(188) 66.2		(226) 79.6		(124) 43.7	
Yes	228	(166) 72.8		(205) 89.9		(141) 61.8	
Age at menopause in years			0.687		0.364		0.374
≤ 44	44	(34) 77.3		(42) 95.5		(23) 52.3	
45-49	75	(55) 73.3		(68) 90.7		(51) 68.0	
50-54	94	(65) 69.2		(81) 86.2		(57) 60.6	
55+	15	(12) 80.0		(14) 93.3		(10) 66.7	
Ever used HRT			0.056		**0.021**		0.465
No	507	(353) 69.6		(429) 84.6		(262) 51.7	
Yes	6	(2) 33.3		(3) 50.0		(4) 66.7	
Cholesterol (mmol/l)			0.647		**0.009**		0.170
Normal	376	(258) 68.6		(307) 81.7		(186) 49.5	
Elevated cholesterol	120	(85) 70.8		(110) 91.7		(68) 56.7	
LDL-Cholesterol (mmol/l)			0.430		**0.042**		0.389
Normal	398	(272) 68.3		(328) 82.4		(200) 50.3	
Elevated LDL-chol	98	(71) 72.5		(89) 90.8		(54) 55.1	

Characteristic	Number of women	Obese BMI ≥ 30kg/m^2 n %	P value	WC ≥ 88 cm, % n %	P-value	W/H ratio ≥ 0.85 cm, % n %	P value
HDL-Cholesterol (mmol/l)			**0.034**		**<0.0001**		**<0.0001**
Decreased HDL-Chol	246	(181) 73.6		(223) 90.7		(150) 61.0	
Normal	250	(162) 64.8		(194) 77.6		(104) 41.6	
Triglyceride (mmol/l)			**0.001**		**<0.0001**		**<0.0001**
Normal	341	(220) 64.5		(270) 79.2		(154) 45.2	
Elevated TG	155	(123) 79.4		(147) 94.8		(100) 64.5	
TChol/HDL-C			0.149		**0.007**		**0.003**
Normal	324	(217) 67.0		(262) 80.9		(150) 46.3	
High risk	172	(126) 73.3		(155) 90.2		(104) 60.5	
DBP mmHg			**0.001**		**<0.0001**		**<0.0001**
Normal	332	(213) 64.2		(261) 78.6		(151) 45.5	
Elevated DBP ≥ 90 mmHg/ or medication	181	(142) 78.5		(171) 94.5		(115) 63.5	
SBP mmHg			**0.002**		**<0.0001**		**<0.0001**
Normal	318	(204) 64.2		(249) 78.3		(139) 43.7	
Elevated SBP ≥ 140 mmHg/or medication	195	(151) 77.4		(183) 93.9		(127) 65.1	
Hypertension			**<0.0001**		**<0.0001**		**<0.0001**
Normal	295	(186) 63.1		(228) 77.3		(130) 44.1	
Hypertensive	218	(169) 77.5		(204) 93.6		(136) 62.4	
Diabetic, % ≥ 1 mmol/l			0.102		**0.004**		**<0.0001**
No	399	(269) 67.4		(326) 81.7		(181) 45.4	
Yes	114	(86) 75.4		(106) 93.0		(85) 74.6	
Central obesity, WC ≥ 88 cm			**<0.0001**				**<0.0001**
Normal	81	(2) 2.5				(18) 22.2	
WC ≥ 88 cm	432	(353) 81.7				(248) 57.4	
BMI					**<0.0001**		**0.037**
Non-obese	158			(79) 50.0		(71) 44.9	
Obese BMI ≥ 30kg/m^2	355			(353) 99.4		(195) 54.9	
Abdominal obesity, W/H ratio ≥ 0.85 cm			0.037		**<0.0001**		
Normal	247	(160) 64.8		(184) 74.5			
WHR ≥ 0.85	266	(195) 73.3		(248) 93.2			

Characteristic	Number of women	Obese BMI ≥ 30kg/m^2 n %	P value	WC ≥ 88 cm, % n %	P-value	W/H ratio ≥ 0.85 cm, % n %	P value
Self rating of obesity			**<0.0001**		**<0.0001**		0.100
Underweight	21	(4) 19.1		(7) 33.3		(11) 52.4	
Normal weight	141	(60) 42.6		(95) 67.4		(66) 46.8	
Overweight	227	(175) 77.1		(207) 91.2		(111) 48.9	
Obese	94	(89) 94.7		(94) 100.0		(60) 63.8	
Very obese	25	(25) 100.0		(25) 100.0		(14) 56.0	

8.1 Further Analysis of Obesity with Parity

In this section, we aim to investigate the hypothesis that an increasing number of children is associated with an increasing risk of obesity among Palestinian women aged 40-65 years independent of socioeconomic status, other reproductive and lifestyle factors. The initial results were shown in sections 7.6 and 7.7 and this section takes the relationship of BMI and parity further. For each of these outcomes, initial results of the relationship with parity and other characteristics of the women were shown in Chapter 7. Here the relationships are explored further with the outcome taken both as proportion above the cut-point for obesity and as a mean, and with explicit allowance for confounders. In the case of BMI and WC measures where a relationship with parity was found, mediation of this relationship via other factors is explored in sections 8.2 and 8.4.

The effect of parity on obesity (BMI $\geq$ 30 kg/m^2) was assessed in a model controlling for the woman's age, education and that of their husbands as well as their marital status as seen in Tables 8-2. For comparison with a "baseline" group, parity 10+ was chosen as the baseline rather than parity 0 because the latter was small in number entailing very limited precision and wide confidence intervals. Comparisons with parity 0 would lack statistical power to detect any association, and the changes in these comparisons between higher parity groups would be less certain. Parity 10+ was a much larger group. The choice of this group as baseline, rather than 7-9 (the group that covers the mean parity) was arbitrary.

Table 8-2: Unadjusted and adjusted odds ratios for the effect of parity in groups on obesity (increased BMI)

Parity	n	% Obese	Obesity (BMI ≥ 30 kg/m2)					
			Unadjusted			Adjusted		
			OR	95% CI		OR		
				Lower	Upper		Lower	Upper
0	42	54.8	0.33	0.16	0.68	0.34	0.12	1.012
1-3	38	63.2	0.47	0.22	1.01	0.46	0.19	1.11
4-6	116	55.2	0.34	0.20	0.58	0.35	0.19	0.63
7-9	164	75.6	0.85	0.50	1.44	0.80	0.46	1.40
10+	153	78.4	1			1		
P-value					< 0.0001			0.0040

Adjustment for age, woman's education, husband's education, and marital status

Table 8-2 shows that there was a strong trend for obesity to increase with increasing parity, p< 0.0001. From the highest parity group, obesity decreased with less parity, but rose slightly at parity 1-3, then decreased at parity 0. The CIs suggests that this slight increase in parity 1-3 is not statistically significant and could be due to chance.

Adjustment did not make much difference in the magnitude of the trend. As in the unadjusted results obesity decreased with less parity, increased at parity 1-3, and then decreased at parity 0. Again, the CI suggests that this slight increase at parity 1-3 is not statistically significant.

When parity was fitted into the regression model as a continuous variable and BMI was kept as a categorical variable, the change in unadjusted odds of BMI ≥ 30 (obesity) per extra child (unit change in parity) was 1.13 (95% CI 1.07 to 1.19, p< 0.0001).

Table 8-3: The change of unadjusted and adjusted odds of BMI ≥ 30 per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.13	.03	1.07	1.19	< 0.0001
Adjusted for age, educational level, husband's years of schooling and marital status (fully adjusted model)	1.14	.04	1.07	1.22	<0.0001

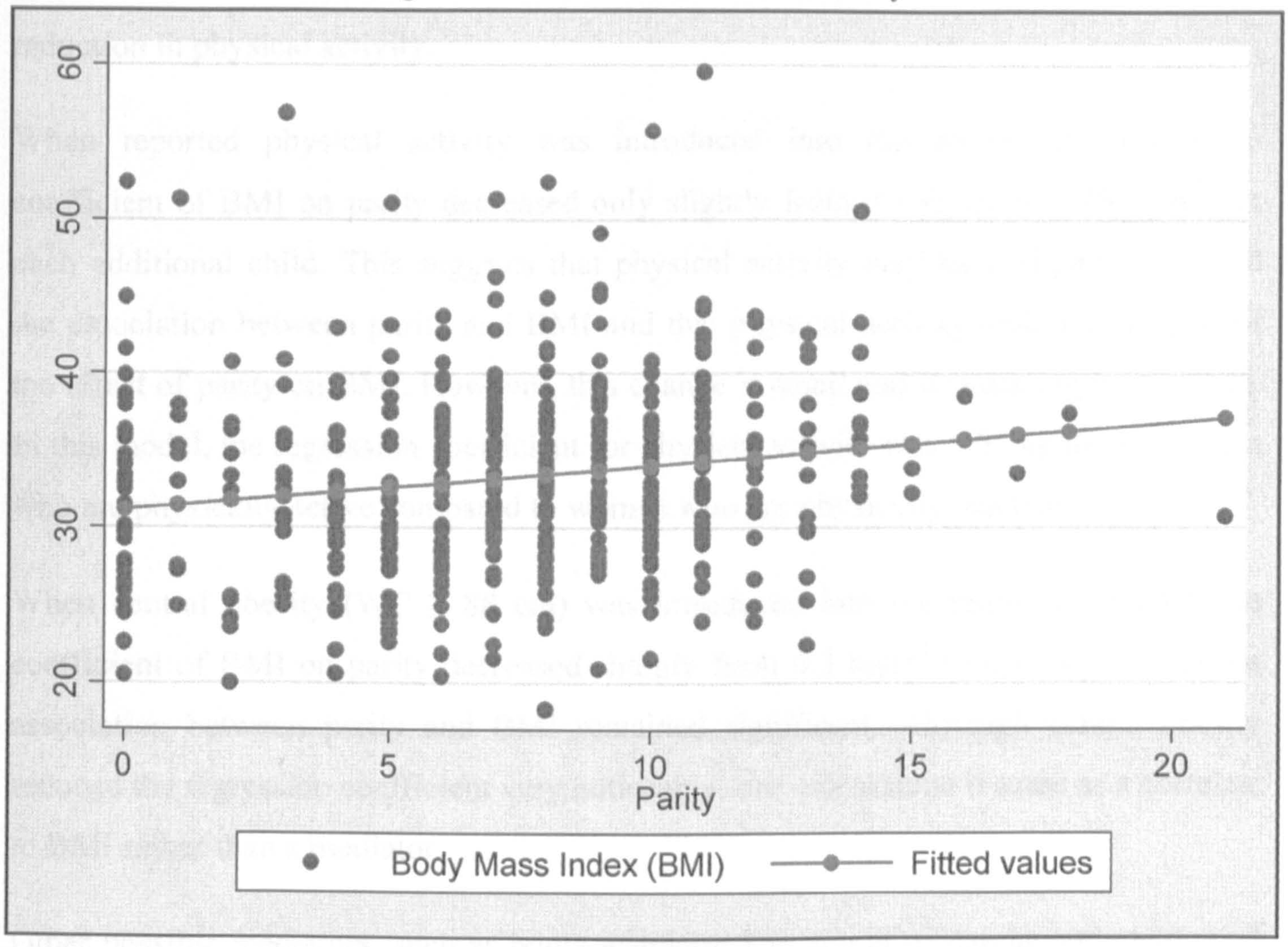
After adjustment for age, women's educational level, husband's years of schooling and marital status, the risk of obesity increased by 14% with each additional live birth.

The relationship between BMI and parity was finally examined with both variables being continuous, using a scatter diagram and by ordinary regression. The regression slope was 0.28 kg/m^2 denoting the predicted increase in BMI for a unit increase in parity. The standard error of this slope was 0.07 and it was significantly different from zero, $p<0.0001$. Adjustment for age, women's educational level, husband's schooling and marital status did not noticeably reduce the magnitude of change, although education did so slightly, but the association between parity and BMI remained significant. The scatter diagram with the fitted line is shown in Figure 8-1 indicating the scatter plot of the two variables BMI and parity with the regression line.

Table 8-4: The unadjusted and adjusted regression slopes of BMI on parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.28	0.07	0.15	0.42	< 0.0001
Adjusted for age, educational level, husband's years of schooling and marital status (fully adjusted)	0.30	0.09	0.14	0.47	<0.0001

Figure 8-1: Scatter Plot of BMI and Parity



This diagram confirms the linear relationship between parity and obesity and suggests strongly that the linear model is adequate.

8.2 Other Characteristics and Mediators:

In the remaining part of this section, we assess the role of mediators that could act along the casual pathway between parity and obesity in the model fully adjusted for age, educational level, husband's schooling and marital status. Results for each mediator are presented in Table 8-5.

Of all the variables thought of as eligible to act as mediators, assistance in housework seems to produce enough change to be considered as a predominant one. When the assistance in housework variable was introduced into the regression model, the regression coefficient of BMI on parity decreased noticeably from 0.30 to 0.23 kg/m^2 per each additional child, suggesting that the influence between parity and BMI is mediated partially by assistance in housework. Moreover, the regression coefficient of BMI was 2.51 kg/m^2 per unit increase (daily) of assistance at housework. It has been

remarked above that assistance in housework reduces physical demands, with resultant reduction in physical activity.

When reported physical activity was introduced into the model, the regression coefficient of BMI on parity decreased only slightly from 0.3 kg/m^2 to 0.28 kg/m^2 per each additional child. This suggests that physical activity may have slightly mediated the association between parity and BMI and that physical activity took a small part of the effect of parity on BMI. However, this change is small and its meaning is uncertain. In this model, the regression coefficient for physical activity was 2.67 kg/m^2 for women who are physically active compared to women who are physically inactive.

When central obesity (WC $\geq$ 88 cm) was introduced into the regression model, the coefficient of BMI on parity decreased sharply from 0.3 kg/m^2 to 0.17 kg/m^2, but the association between parity and BMI remained significant. Although central obesity reduced the regression coefficient very noticeably, one can assume it acted as a correlate to BMI rather than a mediator.

Other possible mediators, such as hours watching TV, age at menarche and abdominal obesity, made only very small changes to the regression coefficient of parity. Hence, their mediating effects were non-existence or slight. Table 8-5 shows potential mediators that can act along the causal pathway between parity and BMI, on the fully adjusted regression coefficient.

Table 8-5: Effect of mediators along the causal pathway between parity & obesity (BMI) on the fully adjusted regression coefficient

Additional characteristics (mediators)	Slope (regression coefficient) for BMI on parity	95% CI		P value	Slope (regression co-efficient) of additional characteristic	95% CI		P value
		Lower	Upper			Lower	Upper	
Unadjusted	0.28	0.145	0.421	<0.0001				
Fully adjusted	0.30	0.137	0.471	<0.0001				
Assistance in house	0.23	0.060	0.400	0.008	2.51	1.30	3.72	<0.0001
Physical activity	0.28	0.112	0.443	0.001	-2.67	-4.221	-1.120	0.001
Hours watching TV	0.31	0.131	.487	0.001	0.066	0.022	0.110	0.003
Age at menarche	0.29	0.121	0.457	0.001	-0.494	-0.872	-0.116	0.011
Central obesity WC	0.17	0.026	0.315	0.021	8.67	7.354	9.993	< 0.0001
Abdominal obesity W/H ratio	0.30	0.128	0.461	0.001	1.17	0.104	2.238	0.032

None of these variables fully mediated the association between parity and obesity suggesting that the association between parity and obesity is real and is independent of any effect of these covariates. This suggests a physiological effect of parity on obesity. Assistance in housework could partially explain some of the effect, yet the association between parity and BMI remained significant.

We conclude that childbearing in addition to life style factors, physical inactivity and leading sedentary habits contributes to obesity in this group of women.

8.3 Further Analysis of Waist Circumference with Parity

In this section, we aim to test the hypothesis that an increasing number of children is associated with increasing waist circumference and therefore increasing central obesity. This association was assessed using the same statistical models as in parity and BMI.

Table 8-6: Unadjusted and adjusted odds ratio for the effect of parity in groups on increased waist circumference

Parity	n	%	Abdominal obesity WC ≥ 88 cm					
			Unadjusted			Adjusted		
			OR	95% CI		OR	95% CI	
				Lower	Upper		Lower	Upper
0	42	73.8	0.24	0.10	0.59	0.42	0.10	1.79
1-3	38	68.4	0.18	0.08	0.46	0.22	0.08	0.65
4-6	116	76.7	0.28	0.14	0.58	0.39	0.17	0.89
7-9	164	88.4	0.65	0.30	1.39	0.79	0.35	1.77
10+	153	92.2	1			1		
P-value					< 0.0001			0.03

Adjustment for age, woman's education, husband's education, and marital status

Table 8-6 shows that there is a strong trend for WC to increase with increasing parity, $p < 0.0001$. Waist circumference decreases with less parity as the odds ratios show, and rises again at parity 0.

The table also shows that adjusted WC decreases with less parity with a slight increase at parity 0. But, as with the analysis for BMI, the CIs suggest that the upward trend from parity 1-3 to parity zero is not statistically significant, so a suggestion of a J-shaped relationship is not supported.

The effect of confounders on the relationship of central obesity and parity is also shown in Table 8-6. In contrast to the results for BMI, there appears to be some weakening of the effect of parity, which however remains definite.

When parity was fitted into the regression model as a continuous variable and WC is kept as a categorical variable as in Table 8-7 the change in odds of WC≥ 88 (central obesity) per extra child (unit change in parity) is 1.18 (95% CI 1.10 to 1.26, p< 0.0001.

Table 8-7: The change of unadjusted and adjusted odds of WC≥ 88 cm per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.18	0.04	1.10	1.26	<0.0001
Adjusted for age, educational level, husband's years of schooling and marital status	1.18	0.06	1.07	1.29	0.001

After adjustment for age, women's educational level, husband's years of schooling and marital status, the risk of central obesity increased by 18% with each additional child. Again, adjustment made very little difference.

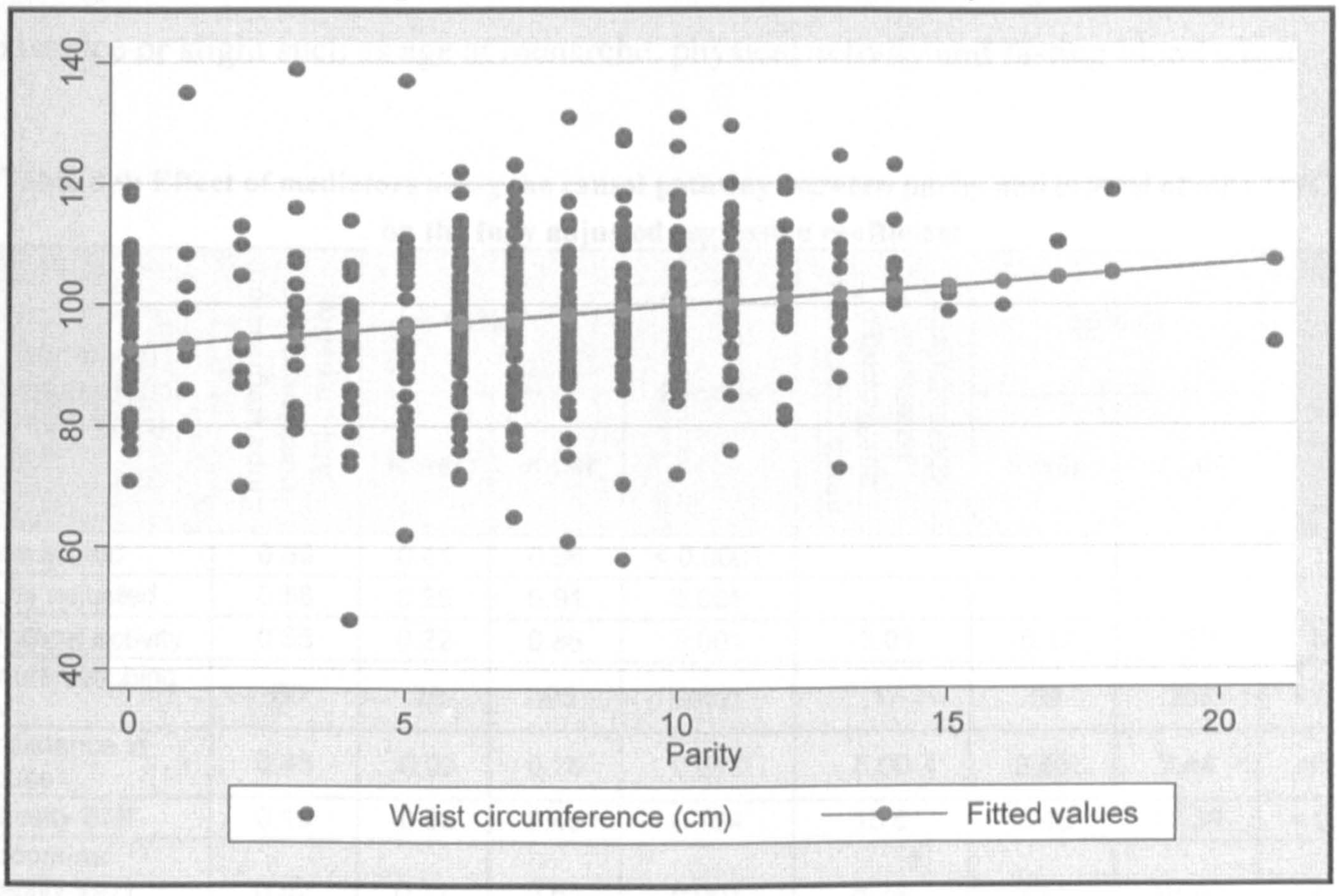
When parity was measured on a continuous scale using ordinary regression the mean WC increased by 0.69 cm per extra child as shown in Table 8-8. When the association was adjusted for confounders, the magnitude of change was reduced slightly to 0.58 but the association remained significant

Table 8-8: The Unadjusted and Adjusted Regression Slopes of WC on Parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.69	0.14	0.41	0.96	< 0.0001
Adjusted for age, educational level, husband's years of schooling and marital status	0.58	0.17	0.25	0.91	0.001

Figure 8-2 shows the scatter plot of the two variables waist circumference and parity with the regression line. The scatter plot suggests strongly that the linear model is adequate, and to represent the relationship of mean WC there is no need to look at parity in groups.

Figure 8-2: Scatter Plot of WC and Parity



8.4 Other Characteristics and Mediators

In this section, potential mediators that could act along the casual pathway between parity and central obesity are assessed in the fully adjusted model for age, educational level, husband's schooling and marital status. Results are presented in Table 8-9. When the assistance in housework variable was introduced into the regression model, the regression coefficient of WC on parity decreased noticeably compared to the effect of the other life-style mediators, except for physical activity. The slope of WC on parity was reduced from 0.58 to 0.43 cm per each additional child, suggesting that some of the influence between WC and parity is mediated partially by assistance in housework. The regression coefficient of assistance in housework was 5.00 cm being the average increase in WC among those who reported assistance in housework compared to women who did not.

Abdominal obesity W/H ratio $\geq$ 0.85 reduces the magnitude of the slope of WC from 0.58 cm to 0.51 cm, but again W/H ratio is a correlate of WC and might not be considered as a mediator.

The same applies to BMI. When obesity (BMI$\geq$ 30 kg/m^2) was introduced into the regression model, the regression coefficient of WC on parity decreased sharply from 0.58 cm to 0.19 cm, and the association between WC and parity disappeared.

Other possible mediators were considered, but their mediating effects were non-existence or slight such as age at menarche, physical activity and fasting blood sugar.

Table 8-9: Effect of mediators along the causal pathway between parity and central obesity (WC) on the fully adjusted regression coefficient

Additional characteristics (mediators)	Slope (regression coefficient) for BMI on parity	95% CI		P-value	Slope (regression coefficient) of additional characteristic	95% CI		P value
		lower	upper			lower	upper	
Unadjusted	0.69	0.41	0.96	< 0.0001				
Fully adjusted	0.58	0.25	0.91	0.001				
Physical activity	0.55	0.22	0.88	0.001	-3.01	-6.12	-.09	0.057
Hours watching TV	.60	.25	.95	0.001	.17	.09	.257	< 0.0001
Assistance in house	0.43	0.09	0.76	0.013	5.00	2.60	7.44	<0.0001
Obesity BMI	0.19	-0.08	0.46	0.164	15.5	13.59	17.36	< 0.0001
Abdominal obesity W/H ratio	0.52	0.21	0.83	0.001	8.24	6.24	10.24	< 0.0001
Fasting blood sugar	.62	.28	.95	< 0.0001	.02	.004	.039	0.016

Assistance in housework seems to carry some of the influence of parity on WC, yet the association between WC and parity remained significant as shown in table 8-9, suggesting that the association could be due to the biological consequences of pregnancy and sedentary lifestyle.

8.5 Further Analysis of the Waist Hip Ratio with Parity

In the following section, we aim to test the hypothesis that an increasing number of children was associated with an increasing waist to hip ratio. The association between parity and waist to hip ratio was assessed using the same statistical models as for parity and BMI.

The relationship between unadjusted and adjusted increased W/H ratio (≥ 0.85) ratio with parity in groups is shown in Table 8-10. All the CIs show no significant association, $p= 0.3891$ and $p= 0.7821$ respectively.

Table 8-10: Unadjusted and adjusted odds ratios for the effect of parity in groups on increased W/H ratio

Parity	n	%	W/H ratio ≥ 0.85					
			Unadjusted			Adjusted		
			OR	95% CI		OR	95% CI	
				Lower	Upper		Lower	Upper
0	42	59.5	1.15	0.57	2.29	0.42	0.10	1.79
1-3	38	42.1	0.57	0.28	1.16	0.22	0.08	0.65
4-6	116	50.0	0.78	0.48	1.26	0.39	0.17	0.89
7-9	164	49.4	0.76	0.49	1.18	0.79	0.35	1.77
10+	153	56.2	1			1		
P-value					0.3891			0.7821

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable and W/H ratio was kept as a categorical variable as in Table 8-11 the change in odds of W/H ratio ≥ 0.85 (abdominal obesity) per extra child (unit change in parity) was 1.026 (95% CI .979 to 1.075, p=0.292).

Table 8-11: The change of unadjusted and adjusted odds of W/H ratio ≥ 0.85 per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.026	0.025	0.979	1.075	0.292
Adjusted for age, educational level, husband's years of schooling and marital status	1.035	0.0320	0.9740	1.010	0.268

After adjustment for confounders age, women's educational level, husband's years of schooling and marital status the association remained non significant. Finally, no statistically significant association was seen when parity was measured on a continuous scale using ordinary regression, see Table 8-12.

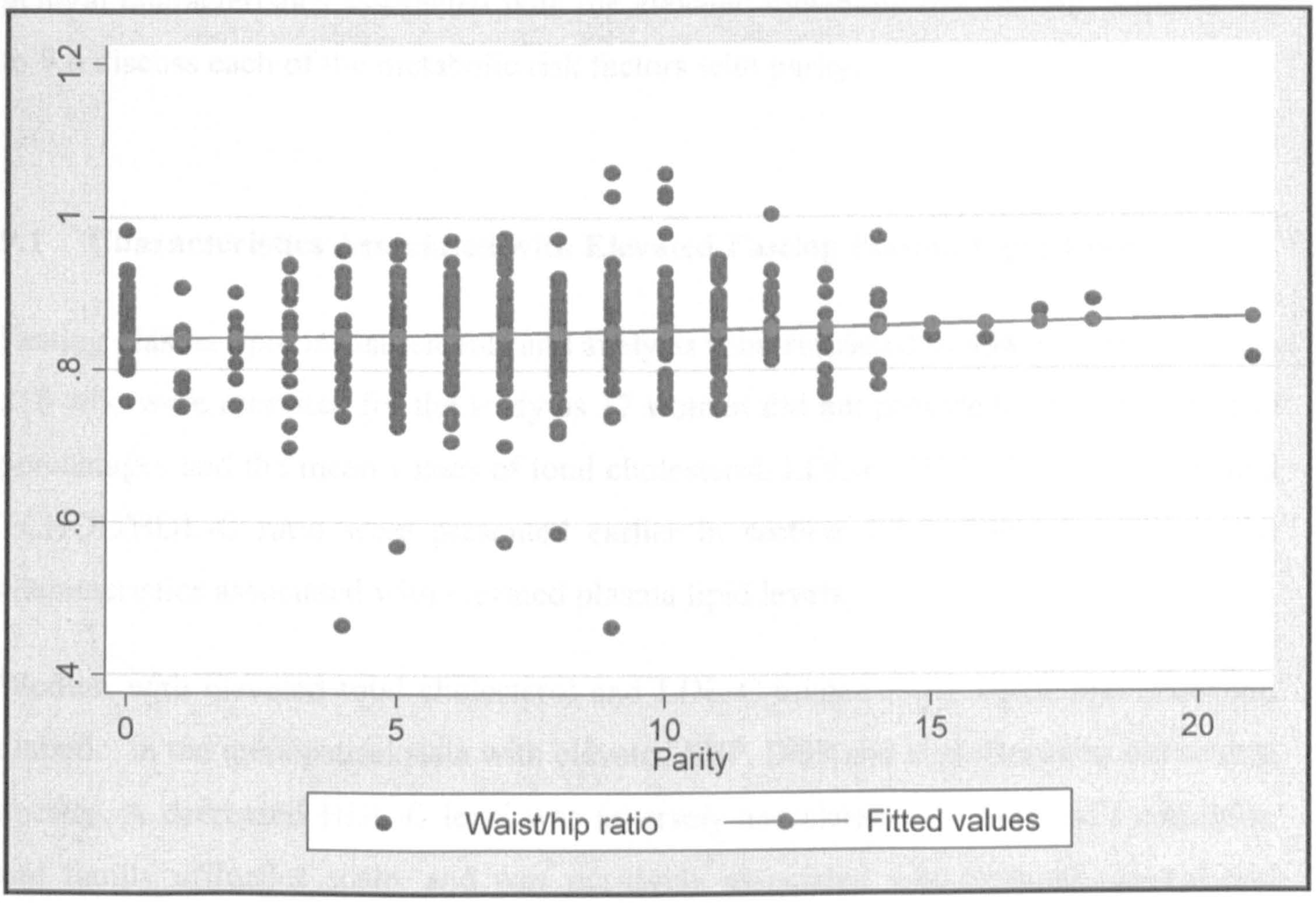
Table 8-12: The Unadjusted and Adjusted Regression Slopes of W/H Ratio on Parity

	Slope	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.0013	0.0008	-0.0002	0.0028	0.090
Adjusted for age, educational level, husband's years of schooling and marital status (fully adjusted)	0.0010	0.0009	-0.0009	0.0028	0.308

Because there was no evidence of any association between parity and W/H ratio, effects of mediators were not investigated.

Figure 8-3 shows the scatter plot of the two variables waist/hip ratio and parity with the regression line at the same level.

Figure 8-3: Scatter Plot of W/H Ratio and Parity



Chapter 9
PARITY AND LIPID LEVELS

One possible pathway by which the number of pregnancies and the number of children could be related to the subsequent development of coronary heart disease is through the alteration of lipid levels. Results on the association between parity and the lipid levels (the metabolic risk factors) are presented in this chapter. Section 9.1 focuses on the general characteristics associated with the elevated metabolic risk factors. Sections 9.2 to 9.6 discuss each of the metabolic risk factors with parity.

9.1 Characteristics Associated with Elevated Fasting Plasma Lipid Levels

Fasting plasma lipid measurements and analysis were restricted to 498 women out of the 515 who were recruited for the study as 17 women did not provide blood samples. The percentages and the mean values of total cholesterol, LDL-C, HDL-C, triglycerides and TCHOL/HDL-C ratio were presented earlier in section 7.4.3. Table 9-1 shows the characteristics associated with elevated plasma lipid levels.

Women with elevated total cholesterol and LDL-C tended to be older, less educated, diabetic, in the menopausal state with elevated SBP, DBP and Hypertension, and central obesity. A decreased HDL-C level was inversely associated with husband's education and family affluence scale, and was positively associated with diabetes, central and abdominal obesity. Women who had assistance in housework tended to have decreased HDL-C level.

In addition, women with elevated triglycerides tended to be unemployed, physically inactive, have ever used oral contraceptive pill, diabetic with elevated BMI, central and abdominal obesity and a family history of diabetes. Women with elevated T-CHOL/HDL-C ratio tended to be less educated, more likely to marry at an early age, diabetic and have elevated central and abdominal obesity.

It is interesting to note that neither parity nor gravidity had a significant association with the elevated plasma lipid levels among the women surveyed. The characteristics potentially associated with elevated fasting plasma lipid levels are presented in Table 9-1.

Table 9-1: Characteristics associated with fasting plasma lipids: number and percentages with elevated T-cholesterol, elevated LDL-C, decreased HDL-C, elevated TG and elevated TCHOL/HDL-C ratio

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♦ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Demographic and socio-economic variables											
Age			***<0.0001***		***<0.0001***		0.684		0.065		0.132
<45	155	(25) 16.1		(22) 14.2		(76) 49.0		(36) 23.2		(41) 26.5	
45-49	111	(18) 16.2		(12) 10.8		(60) 54.1		(40) 36.0		(43) 38.7	
50.54	106	(31) 29.3		(26) 24.5		(55) 51.9		(36) 34.0		(40) 37.7	
55-59	91	(35) 38.5		(31) 34.1		(41) 45.1		(28) 30.8		(35) 38.5	
60+	34	(12) 35.3		(8) 23.5		(15) 44.1		(15) 44.1		(14) 41.2	
Women's education, %			***0.010***		***0.040***		0.210		0.103		***0.012***
No formal education	113	(34) 30.1		(27) 23.9		(61) 54.0		(39) 34.5		(42) 37.2	
Elementary	195	(56) 28.7		(46) 23.6		(99) 50.8		(63) 32.3		(78) 40.0	
Secondary	162	(28) 17.3		(24) 14.8		(78) 48.2		(50) 30.9		(50) 30.9	
Higher education	28	(3) 10.7		(2) 7.1		(9) 32.1		(3) 10.7		(3) 10.7	
Marital status, %			0.647		0.780		0.970		0.389		0.999
Married	371	(92) 24.8		(74) 20.0		(184) 49.6		(123) 33.2		(129) 34.8	
Single	21	(4) 19.1		(3) 14.3		(10) 47.6		(6) 28.6		(7) 33.3	
Divorced/separated	26	(4) 15.4		(4) 15.4		(14) 53.9		(7) 26.9		(9) 34.6	
Widowed	80	(21) 26.3		(18) 22.5		(39) 48.8		(19) 23.8		(28) 35.0	
Currently employed			0.516		0.361		***0.071***		***0.024***		***0.034***
No	423	(105)24.8		(87) 20.6		(217) 51.3		(140) 33.1		(155) 36.6	
Yes	75	(16) 21.3		(12) 16.0		(30) 40.0		(15) 20.0		(18) 24.0	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♣ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Occupation			0.505		0.504		0.665		0.308		0.522
Unskilled worker	15	(3) 20.0		(2) 13.3		(8) 53.3		(4) 26.7		(4) 26.7	
Skilled worker	13	(1) 7.7		(1) 7.7		(5) 38.5		(1) 7.7		(4) 30.8	
Employee	23	(5) 21.7		(3) 13.0		(9) 39.1		(3) 13.0		(3) 13.0	
Private business	24	(7) 29.2		(6) 25.0		(8) 33.3		(7) 29.2		(7) 29.2	
Husband's education			0.188		0.514		***0.006***		0.235		***0.019***
No formal education	80	(27) 33.8		(18) 22.5		(44) 55.0		(24) 30.0		(32) 40.0	
Elementary	161	(40) 24.8		(37) 23.0		(84) 52.2		(56) 34.8		(60) 37.3	
Secondary	167	(35) 21.0		(28) 16.8		(86) 51.5		(53) 31.7		(62) 37.1	
Higher education	55	(13) 23.6		(12) 21.8		(15) 27.3		(11) 20.0		(9) 16.4	
Husband currently employed			0.618		0.927		0.943		0.174		0.606
Yes	237	(55) 23.2		(46) 19.4		(116) 49.0		(82) 34.6		(78) 32.9	
No	134	(37) 27.6		(28) 20.9		(68) 50.8		(41) 30.6		(51) 38.1	
Not applicable	106	(250 23.6		(22) 20.8		(53) 50.0		(26) 24.5		(37) 34.9	
Own automatic washing machine			***0.008***		0.086		0.081		0.828		0.243
No	389	(84) 21.6		(71) 18.3		(201) 51.7		(122) 31.4		(130) 33.4	
Yes	109	937) 33.9		(28) 25.7		(46) 42.2		(33) 30.3		(43) 39.5	
Family affluence scale			0.160		0.699		***0.031***		0.995		0.902
Poor	220	(51) 23.2		(47) 21.4		(120) 54.6		(68) 30.9		(78) 35.5	
Average	157	(33) 21.0		(28) 17.8		(79) 50.3		(49) 31.2		(55) 35.0	
Better off	121	(37) 30.6		(24) 19.8		(48) 39.7		(38) 31.4		(40) 33.1	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♣ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Behavioural Risk Factors											
Physical activity			0.984		0.509		0.072		***0.030***		0.168
No	431	(104)24.1		(83) 19.3		(221) 51.3		(142) 33.0		(155) 36.0	
Yes	66	(16) 24.2		(15) 22.7		(26) 39.4		(13) 19.7		(18) 27.3	
Smoking habits			0.326		0.669		0.065		0.730		0.107
Never smoked	465	(111)23.9		(91) 19.6		(226) 48.6		(146) 31.4		(158) 34.0	
Current smoker	27	(7) 25.9		(6) 22.2		(19) 70.4		(8) 29.6		(14) 51.9	
Ex-smoker	6	(3) 50.0		(2) 33.3		(2) 33.3		(1) 16.7		(1) 16.7	
Watch TV			0.188		0.910		0.317		0.687		0.710
No	29	(10) 34.5		(6) 20.7		(17) 58.6		(10) 34.5		(11) 37.9	
Yes	469	(111)23.7		(93) 19.8		(230) 49.0		(145) 30.9		(162) 34.5	
Hours/week watch TV			***0.010***		***0.016***		0.143		0.400		0.662
≤ 4	23	(10) 43.5		(9) 39.1		(8) 34.8		(10) 43.5		(10) 43.5	
5-10	145	(25) 17.2		(23) 15.9		(78) 53.8		(39) 26.9		(49) 33.8	
11-20	130	(27) 20.8		(20) 15.4		(56) 43.1		(41) 31.5		(41) 31.5	
21+	171	(49) 28.7		(41) 24.0		(88) 51.5		(55) 32.2		(62) 36.3	
Assistance in house-work			0.230		0.065		***0.020***		0.120		0.144
No	132	(27) 20.5		(19) 14.4		(54) 40.9		(34) 25.8		(39) 29.6	
Yes	366	(94) 25.7		(80) 21.9		(123) 52.7		(121) 33.1		(134) 36.6	
Stress level			0.057		0.060		0.562		0.594		0.268
No	143	30.1		(36) 25.2		(68) 47.6		(47) 32.9		(55) 38.5	
Yes	355	22.0		(63) 17.8		(179) 50.4		(108) 30.4		(118) 33.2	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♣ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Reproductive Health Factors											
Parity			0.485		0.246		0.881		0.213		0.227
0	40	(7) 17.5		(4) 10.0		(20) 50.0		(11) 27.5		(10) 25.0	
1-3	33	(7) 21.2		(5) 15.2		(14) 42.4		(6) 18.2		(8) 24.2	
4-6	111	(28) 25.2		(22) 19.8		(54) 48.7		(32) 28.8		(39) 35.1	
7-9	161	(35) 21.7		(30) 18.6		(79) 49.1		(49) 30.4		(54) 33.5	
10+	153	(44) 28.8		(38) 24.8		(80) 52.3		(57) 37.3		(62) 40.5	
Age at 1st marriage,			0.280		0.477		0.157		0.180		***0.025***
<18	228	(61) 26.8		(49) 21.5		(121) 53.1		(78) 34.2		(91) 39.9	
18+	249	(56) 22.5		(47) 18.9		(116) 46.6		(71) 28.5		(75) 30.1	
Age at 1st birth			0.414		0.807		0.172		0.299		0.082
≤ 18	169	(46) 27.2		(36) 21.3		(91) 53.9		(58) 34.3		(69) 40.8	
> 18	290	(69) 23.8		(59) 20.3		(137) 47.2		(86) 29.7		(95) 32.8	
Gravidity 5			0.396		0.402		0.999		0.103		0.235
0	36	(5) 13.9		(4) 11.1		(18) 50.0		(10) 27.8		(8) 22.2	
1- 3	29	(9) 31.0		(4) 13.8		(14) 48.3		(4) 13.8		(9) 31.0	
4- 6	60	(12) 20.0		(10) 16.7		(30) 50.0		(16) 26.7		(17) 28.3	
7- 9	131	(31) 23.7		(26) 19.9		(64) 48.9		(38) 29.0		(45) 34.4	
10+	242	(64) 26.5		(55) 22.7		(121) 50.0		(87) 36.0		(94) 38.8	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♣ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Age at menarche			0.644		0.988		0.647		0.283		0.724
≤ 11	37	(7) 18.9		(7) 18.9		(17) 46.0		(8) 21.6		(16) 43.2	
12	105	(25) 23.8		(22) 21.0		(56) 53.3		(41) 39.1		(36) 34.3	
13	132	(36) 27.3		(26) 19.7		(67) 50.8		(39) 29.6		(43) 32.6	
14	131	(34) 26.0		(24) 18.3		(58) 44.3		(40) 30.5		(43) 32.8	
15+	87	(17) 19.5		(18) 20.7		(45) 51.7		(25) 28.7		(33) 37.9	
History of infertility			0.432		0.059		0.801		0.602		***0.045***
No	427	(107)25.1		(91) 21.3		(213) 49.9		(135) 31.6		(155) 36.3	
Yes	50	(10) 20.0		(5) 10.0		(24) 48.0		(14) 28.0		(11) 22.0	
Pregnancy ended as abortion or miscarriage			0.850		0.477		0.189		0.678		0.792
No	156	(40) 25.6		(35) 22.4		(84) 53.9		(47) 30.1		(57) 36.5	
Yes	306	(67) 24.8		(60) 19.6		(145) 47.4		(98) 32.0		(108) 35.3	
Pregnancy ended as a stillbirth			0.320		0.307		0.066		0.515		0.120
No	399	(97) 24.3		(79) 19.8		(191) 47.9		(123) 30.8		(137) 34.3	
Yes	63	(19) 30.2		(16) 25.4		(38) 60.3		(22) 34.9		(28) 44.4	
Have you ever had polycystic ovaries			0.848		0.844		0.429		0.797		0.494
No	478	(116)23.1		(94) 19.7		(240) 50.2		(149) 31.2		(170) 35.6	
Yes	13	(3) 24.3		(3) 23.1		(5) 38.5		(4) 30.8		(3) 23.1	
Ever use CP			0.062		***0.044***		0.944		***0.041***		0.085
No	293	(62) 21.2		(49) 16.7		(146) 49.8		(81) 27.7		(93) 31.7	
Yes	204	(58) 28.4		(49) 24.0		(101) 49.5		(74) 36.3		(80) 39.2	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♣ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Have your periods stopped now			***<0.0001***		***0.001***		0.665		0.163		0.119
No	278	(48) 17.3		(40) 14.4		(140) 50.4		(79) 28.4		(88) 31.7	
Yes	219	(72) 32.9		(58) 26.5		(106) 48.4		(75) 34.3		(84) 38.4	
Age at menopause in years			0.101		0.056		0.163		0.566		0.560
≤ 44	42	(14) 33.3		(9) 21.4		(17) 40.5		(12) 28.6		(19) 45.2	
45-49	72	(17) 23.6		(15) 20.8		(39) 54.2		(23) 31.9		(24) 33.3	
50-54	90	(33) 36.7		(26) 28.9		(46) 51.1		(33) 36.7		(34) 37.8	
55+	15	(8) 53.3		(8) 53.3		(4) 26.7		(7) 46.7		(7) 46.7	
Ever used HRT			0.604		0.406		0.423		0.906		0.350
No	492	(119)24.2		(97) 19.7		(245) 49.8		(153) 31.0		(172) 35.0	
Yes	6	(2) 33.3		(2) 33.3		(2) 33.3		(2) 33.3		(1) 16.7	
Metabolic Factors											
Cholesterol (mmol/L)					***<0.0001***		0.998		***<0.0001***		***<0.0001***
Normal	377			(8) 2.1		(187) 49.6		(95) 25.2		(92) 24.4	
Elevated cholesterol	121			(91) 75.2		(60) 49.6		(60) 49.6		(81) 66.9	
LDL-Cholesterol (mmol/L)			***<0.0001***				***0.046***		***<0.0001***		***<0.0001***
Normal	399	(30) 7.5				(189) 47.4		(101) 25.3		(95) 23.8	
Elevated LDL-chol	99	(91) 91.9				(58) 58.6		(54) 54.6		(78) 78.8	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♦ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
HDL-Cholesterol (mg/dl)			0.998		***0.046***				***<0.0001***		***<0.0001***
Decreased HDL-Chol	247	(60) 24.3		(58) 23.5				(117) 47.4		(152) 61.5	
Normal	251	(61) 24.3		(41) 16.3				(38) 15.1		(21) 8.4	
Triglyceride (mmol/L)			***<0.0001***		***<0.0001***		***<0.0001***				***<0.0001***
Normal	343	(61) 17.8		(45) 13.1		(130) 37.9				(66) 19.2	
Elevated TG	155	(60) 38.7		(54) 34.8		(117) 75.5				(107) 69.0	
TChol/ LDH-chol			***<0.0001***		***<0.0001***		***<0.0001***		***<0.0001***		
Normal	325	(40) 12.3		(21) 6.5		(95) 29.2		(48) 14.8			
High risk	173	(81) 46.8		(78) 45.1		(152) 87.9		(107) 61.9			
DBP mmHg			***0.050***		0.067		0.124		***0.027***		0.920
Normal	321	(69) 21.5		(56) 17.5		(151) 47.0		(89) 27.7		(111) 34.6	
Elevated DBP ≥ 90 mmHg/medication	177	(52) 29.4		(43) 24.3		(96) 54.2		(66) 37.3		(62) 35.0	
SBP mmHg			***0.001***		***0.009***		0.745		***0.030***		0.999
Normal	308	(60) 19.5		(50) 16.2		(151) 49.0		(85) 27.6		(107) 34.7	
Elevated SBP ≥ 140 mmHg/medication	190	(61) 32.1		(49) 25.8		(96) 50.5		(70) 36.8		(66) 34.7	
Hypertension			***0.003***		***0.016***		0.670		***0.036***		0.850
Normal	285	(55) 19.3		(46) 16.1		(139) 48.8		(78) 27.4		(100) 35.1	
Hypertensive SBP/DBP ≥ 140/90 mmHg or on medication	213	(66) 31.0		(53) 24.9		(108) 50.7		(77) 36.2		(73) 34.3	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L‡ n %	P	TG ♣ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Diabetic, % ≥ *7mmol/L or on medication*			***0.016***		***0.001***		***0.003***		***<0.0001***		***<0.0001***
No	400	(88) 22.0		(68) 17.0		(185) 46.3		(99) 24.8		(122) 30.5	
Yes	98	(33) 33.7		(31) 30.6		(62) 63.3		(56) 57.1		(51) 52.0	
Anthropometric Factors											
Central obesity, waist circum ≥ 88 cm			***0.009***		***0.042***		***<0.0001***		***<0.0001***		***0.007***
Normal	79	(10) 12.7		(9) 11.4		(23) 29.1		(8) 10.1		(17) 21.5	
WC ≥ *88 cm*	417	(110) 26.4		(89) 21.3		(223) 53.5		(147) 35.3		(155) 37.2	
BMI			0.647		0.430		***0.034***		***0.001***		0.149
Non-obese	153	(35) 22.9		(27) 17.7		(65) 42.5		(32) 20.9		(46) 30.1	
Obese BMI ≥30kg/m^2	343	(85) 24.8		(71) 20.7		(181) 52.8		(123) 35.9		(126) 36.7	
Abdominal obesity, W/H ratio ≥ 0.85 cm			0.170		0.389		***<0.0001***		***<0.0001***		***0.003***
Normal	242	(52) 21.5		(44) 18.2		(96) 39.7		(55) 22.7		(68) 28.1	
WHR ≥ *0.85*	254	(68) 26.8		(54) 21.3		(150) 59.1		(100) 39.4		(104) 40.9	
Self rating of obesity			0.411		0.425		0.522		0.510		0.723
Underweight	20	(2) 10.0		(2) 10.0		(10) 50.0		(3) 15.0		(7) 35.0	
Normal weight	137	(32) 23.4		(23) 16.8		(62) 45.3		(42) 30.7		(42) 30.7	
Overweight	218	(58) 26.6		(46) 21.1		(106) 48.6		(67) 30.7		(76) 34.9	
Obese	93	(24) 25.8		(23) 24.7		(51) 54.8		(33) 35.5		(37) 39.8	
Very obese	25	(4) 16.0		(4) 16.0		(15) 60.0		(8) 32.0		(9) 36.0	

Characteristics	Number of women	T-chol mmol/L* n %	P	LDL-C† mmol/L N %	P	HDL-C mmol/L♦ n %	P	TG ♣ mmol/L n %	P	Tchol/hdl Mmol/L♪ n %	P
Family history of diabetes			0.463		0.290		0.289		***0.044***		0.273
No history	290	(67) 23.1		(53) 18.3		(138) 47.6		(80) 27.6		(95) 32.8	
Yes	208	(54) 26.0		(46) 22.1		(109) 52.4		(75) 36.1		(78) 37.5	

* Tchol: elevated total cholesterol > 5.2 mmol/L (200 mg/dl), %
† LDL-C: elevated LDL-C > 3.5 mmol/L (135 mg/dl), %
♦ HDL-C: Decreased HDL-C < 1mmol/L (40 mg/dl), %
♣ TG: elevated Triglycerides ≥ 1.7 mmol/L (150 mg/dl), %
♪ Tcholhdl ratio: elevated tcholhdl > 0.13 mmol/L (5 mg/dl), %

The following sections, 9.2 to 9.7, test for and examine the relationships between increasing parity and Total Cholesterol, LDL-C, HDL-C, Triglycerides and the Total Cholesterol to HDL-C ratio. For each of these outcomes, initial results of the relationship with parity and other characteristics of the women were shown in Chapter 7. Here the relationships are explored further with the outcome taken both as proportion above (and below) the cut-point for normality and as a mean, and with explicit allowance for confounders, the same way as was done for parity and BMI and other anthropometric outcomes. In the case of Triglycerides, where a relationship with parity was found, mediation of this relationship via other factors is explored in section 9.6

9.2 Total Cholesterol with Parity

Table 9-2 shows the unadjusted and adjusted association between raised cholesterol level and grouped parity. At no stage of this analysis was the association statistically significant and all the CIs confirm this.

Table 9-2: Unadjusted and adjusted odds ratios for the effect of parity in groups on raised Cholesterol level

Parity	n	%	Raised Total Cholesterol mmol/L					
			Unadjusted			Adjusted		
			OR	95% CI		OR		
				Lower	Upper		Lower	Upper
0	40	17.5	0.53	0.22	1.28	0.65	0.16	2.60
1-3	33	21.2	0.67	0.27	1.65	1.05	0.38	2.90
4-6	111	25.2	0.84	0.48	1.45	1.08	0.58	2.02
7-9	161	21.7	0.69	0.41	1.15	0.84	0.49	1.46
10+	153	28.8	1			1		
P-value					0.490			0.898

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable and T-Cholesterol level was kept as a categorical variable as in Table 9-3, the change in odds of T-Chol > 5.2 mmol/L per extra child (unit change in parity) was 1.04 (95% CI 0.99 to 1.11, p=0.123). With adjustment for age, women's educational level, husband's years of schooling and marital status it remained non significant.

Table 9-3: The change of unadjusted and adjusted odds of T-Cholesterol > 5.2 mmol/L per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.04	0.03	0.99	1.11	0.123
Adjusted for age, educational level, husband's years of schooling and marital status	1.00	0.04	0.94	1.08	0.928

With parity and Total Cholesterol both measured on continuous scales, using ordinary regression, the association was still not significant, unadjusted or adjusted, as shown in Table 9-4.

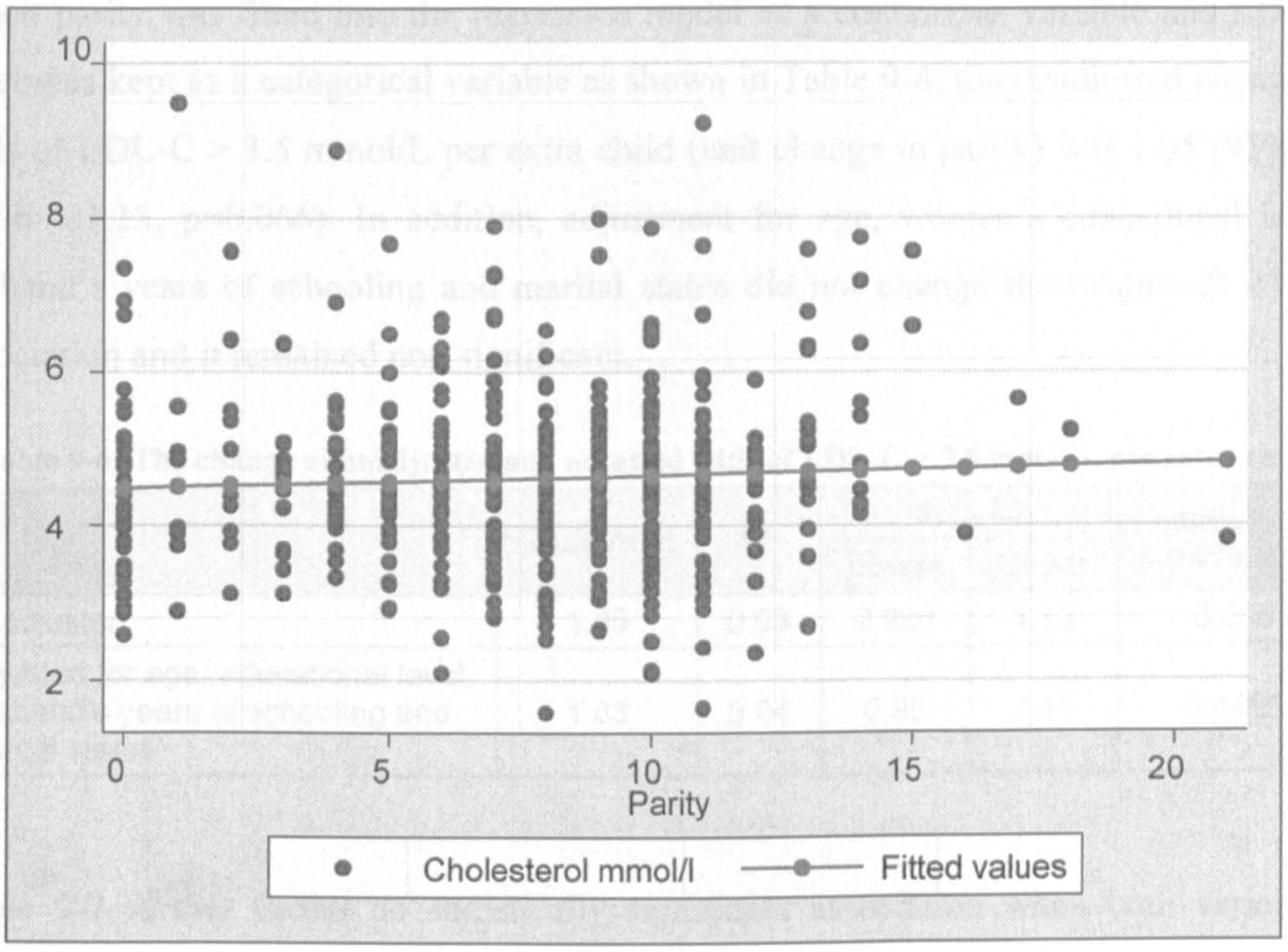
Table 9-4: The unadjusted and adjusted regression slopes of T-Chol (mmol/L) on parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.016	0.014	-0.011	0.043	0.25
Adjusted for age, educational level, husband's years of schooling and marital status	-0.001	0.017	-0.034	0.032	0.946

Since there was no evidence for an association between T-Cholesterol and parity, the effects of mediators were ignored. No evidence was found of an association between gravidity and total cholesterol.

Figure 9-1 below shows the scatter plot of the two variables Total Cholesterol and parity with the regression line.

Figure 9-1: Scatter plot of Total Cholesterol and Parity



9.3 LDL-C with Parity

Table 9-5 shows the unadjusted and adjusted relationships between raised LDL-C level and parity in groups. Neither was significant (p= 0.264, and 0.699 respectively), supported by the confidence intervals.

Table 9-5: Unadjusted and adjusted odds ratios for the effect of grouped parity on raised LDL-C levels

Parity	n	%	Raised LDL-C mmol/l					
			Unadjusted			Adjusted		
			OR	95% CI		OR		
				Lower	Upper		Lower	Upper
0	40	10.0	0.34	0.11	1.01	0.23	0.03	1.87
1-3	33	15.2	0.54	0.20	1.50	0.75	0.24	2.33
4-6	111	19.8	0.75	0.41	1.35	0.86	0.44	1.67
7-9	161	18.6	0.69	0.40	1.19	0.82	0.46	1.46
10+	153	24.8	1			1		
P-value					0.264			0.699

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable and LDL-C level was kept as a categorical variable as shown in Table 9-6, the unadjusted change in odds of LDL-C > 3.5 mmol/L per extra child (unit change in parity) was 1.05 (95% CI 0.996 to1.13, p=0.066). In addition, adjustment for age, women's educational level, husband's years of schooling and marital status did not change the magnitude of the association and it remained non significant.

Table 9-6: The change of unadjusted and adjusted odds of LDL-C > 3.5 mmol/L per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.05	0.03	0.996	1.13	0.066
Adjusted for age, educational level, husband's years of schooling and marital status	1.03	0.04	0.95	1.11	0.0485

Table 9-7 further shows no statistically significant association when both variables, parity and LDL-C, were taken on a continuous scale, using ordinary regression.

Table 9-7: The unadjusted and adjusted regression slopes of LDL-C (mmol/L) on parity

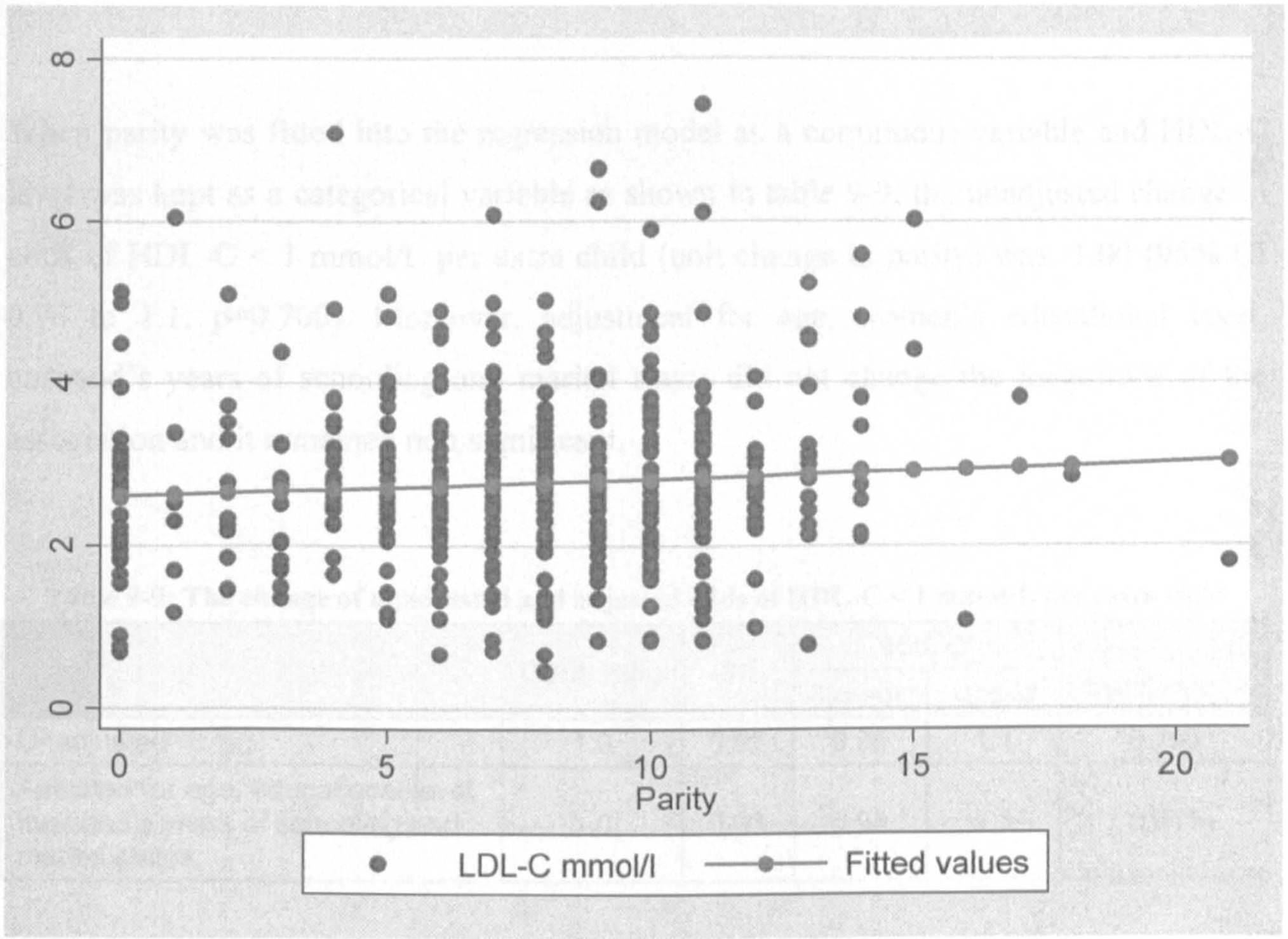
	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.021	0.013	-0.004	0.046	0.104
Adjusted for age, educational level, husband's years of schooling and marital status	0.004	0.016	-0.028	0.033	0.817

The effect of mediators was not considered in a further analysis as an existing association between parity and LDL-C level was not evident.

The same conclusions applied to the association between gravidity and LDL-C (detailed results not shown).

Figure 9-2 shows the scatter plot of the two variables LDL-C and parity with the regression line

Figure 9-2: Scatter Plot of LDL-C and Parity



9.4 HDL-C with Parity

Table 9-8 shows the unadjusted and adjusted odds ratios (OR) for the effect of parity on decreased HDL-C level. It reveals no statistically significant association, (p=0.882 and 0.951 respectively).

Table 9-8: Unadjusted and adjusted odds ratios for the effect of grouped parity on decreased HDL-C levels

Parity	n	%	HDL-C < 1 mmol/l					
			Unadjusted			Adjusted		
			OR	95% CI		OR		
				Lower	Upper		Lower	Upper
0	40	50.0	0.91	0.46	1.83	0.82	0.29	2.3
1-3	33	57.6	0.67	0.32	1.44	0.82	0.34	1.9
4-6	111	51.4	0.86	0.53	1.41	1.0	0.59	1.7
7-9	161	50.9	0.88	0.57	1.37	0.87	0.54	1.4
10+	153	47.7	1			1		
P-value					0.882			0.951

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable and HDL-C level was kept as a categorical variable as shown in table 9-9, the unadjusted change in odds of HDL-C < 1 mmol/L per extra child (unit change in parity) was 1.00 (95% CI 0.96 to 1.1, p=0.700). Moreover, adjustment for age, women's educational level, husband's years of schooling and marital status did not change the magnitude of the association and it remained non significant.

Table 9-9: The change of unadjusted and adjusted odds of HDL-C < 1 mmol/L per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.0	0.02	0.96	1.1	0.700
Adjusted for age, educational level, husband's years of schooling and marital status	1.0	0.03	0.94	1.1	0.911

With HDL_C and parity was measured on continuous scales, using ordinary regression, HDL-C decreased by 0.006 mmol/l per extra child, but this association was not statistically significant (95% CI -0.013 to 0.001, p= 0.093). After adjustment for confounders the association remained not significant as seen in Table 9-10.

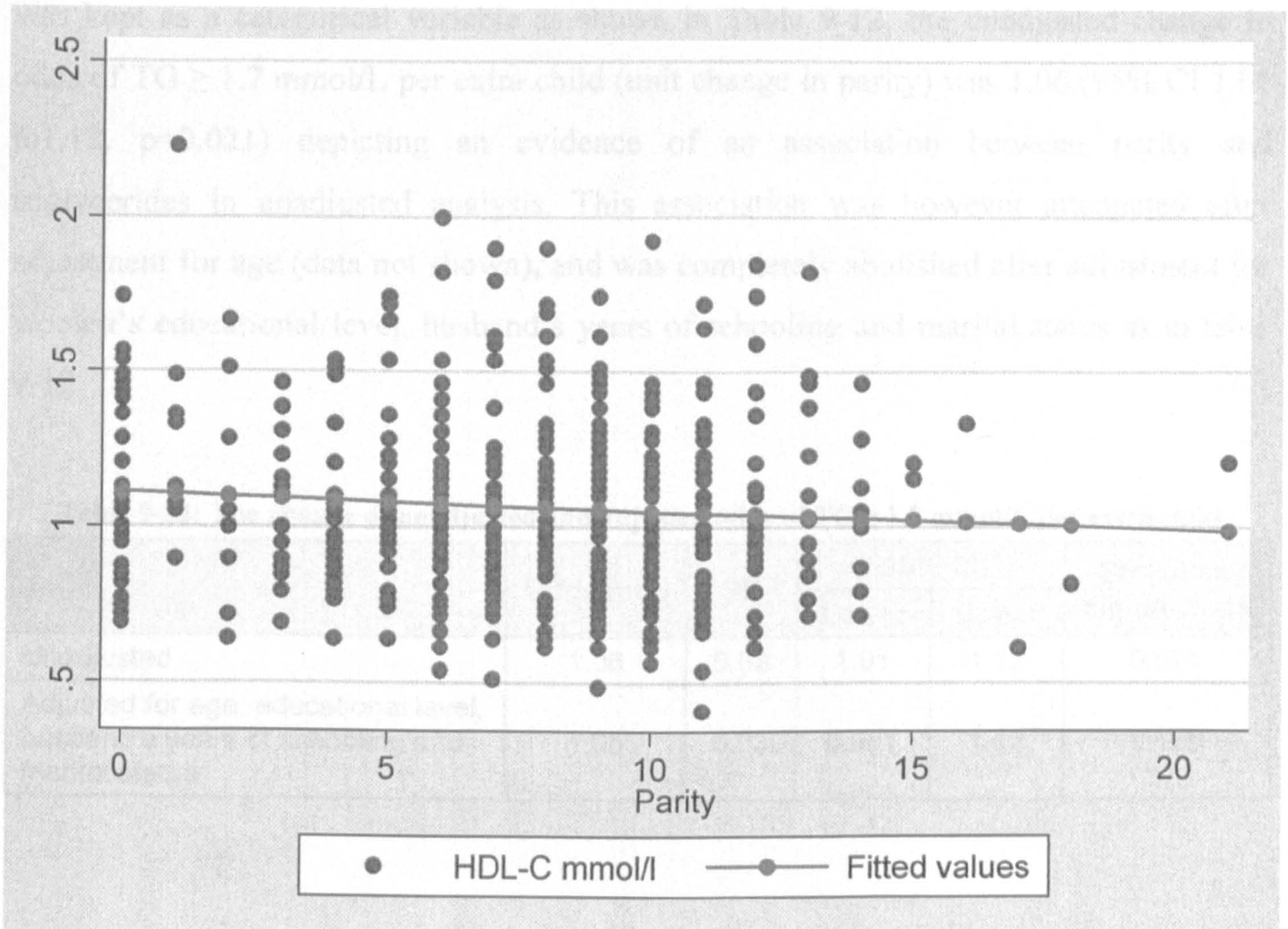
Table 9-10: The unadjusted and adjusted regression slopes of HDL-C (mmol/L) on parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	-0.006	0.004	-0.013	0.001	0.093
Adjusted for age, educational level, husband's years of schooling and marital status	-0.005	0.004	-0.014	0.004	0.267

In the absence of a statistical association in the above analyses, analysis of mediators is not presented.

Figure 9-3 shows the scatter plot of the two variables HDL-C and parity with the regression line.

Figure 9-3: Scatter Plot of HDL-C and Parity



9.5 Triglycerides with Parity

Table 9-11 shows the unadjusted and adjusted relationship between raised triglycerides and parity in groups, which was insignificant, (p= 0.225 and 0.658 respectively).

Table 9-11: Unadjusted and adjusted odds ratios for the effect of grouped parity on raised Triglycerides (TG) levels

Parity	n	%	Raised Triglycerides mmol/L					
			Unadjusted			Adjusted		
			OR	95% CI		OR		
				Lower	Upper		Lower	Upper
0	40	27.5	0.64	0.30	1.38	0.78	0.25	2.46
1-3	33	18.6	0.37	0.15	0.96	0.48	0.17	1.35
4-6	111	28.8	0.68	0.40	1.15	0.84	0.47	1.51
7-9	161	30.4	0.74	0.46	1.18	0.78	0.47	1.28
10+	153	37.3	1			1		
P-value					0.225			0.658

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable and TG level was kept as a categorical variable as shown in Table 9-12, the unadjusted change in odds of TG $\geq$ 1.7 mmol/L per extra child (unit change in parity) was 1.06 (95% CI 1.01 to1.12, p=0.021) depicting an evidence of an association between parity and triglycerides in unadjusted analysis. This association was however attenuated after adjustment for age (data not shown), and was completely abolished after adjustment for women's educational level, husband's years of schooling and marital status as in table 9-12.

Table 9-12: The change of unadjusted and adjusted odds of TG $\geq$ 1.7 mmol/L per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.06	0.03	1.01	1.12	0.021
Adjusted for age, educational level, husband's years of schooling and marital status	1.05	0.03	0.981	1.12	0.169

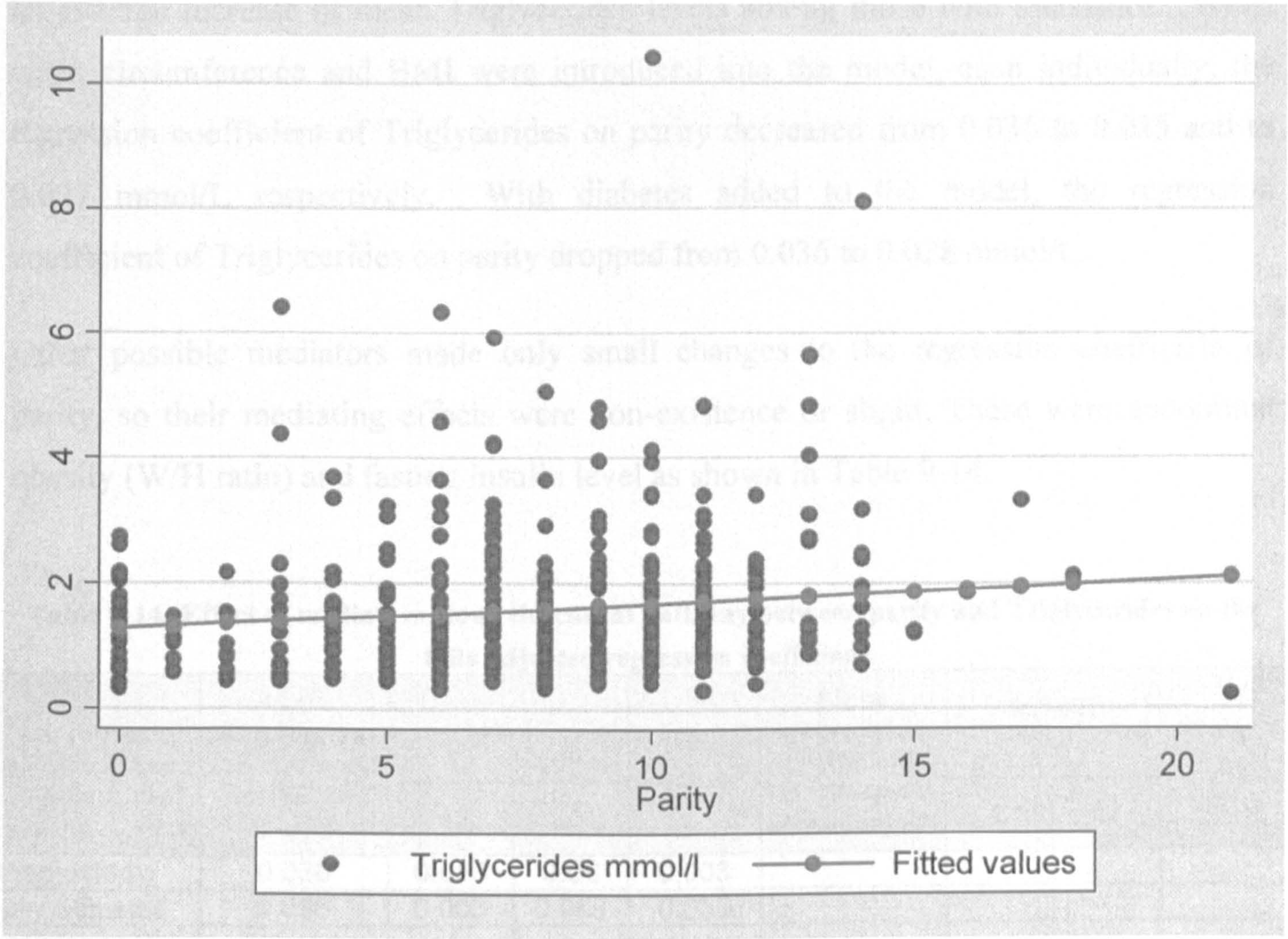
With parity and triglycerides measured on continuous scales, using ordinary regression, mean TG increased by 0.038 mmol/L per extra child, p= 0.003. Adjustment for age, woman's education and husband years of schooling and marital status reduced slightly the magnitude of change in mean TG, but the association remained significant as in shown in Table 9-13.

Table 9-13: The unadjusted and adjusted regression slopes of TG (mmol/L) on parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.038	0.013	0.013	0.06	0.003
Adjusted for age, educational level, husband's years of schooling and marital status	0.036	0.017	0.003	0.068	0.033

Figure 9-4 shows the scatter plot of TG and parity with the regression line.

Figure 9-4: Scatter Plot of Triglycerides and Parity



There was also an association between gravidity and Triglycerides, when the latter was regressed on gravidity using the fully adjusted model, the regression coefficient was 0.033 mmol/L, with a S.E. of 0.013 (95% CI 0.007 to 0.059, p= 0.013).

9.6 Mediators of the Parity-Triglyceride relationship

We now assess the role of mediators that could act along the casual pathway between parity and Triglycerides in the model fully adjusted for the confounders, age, educational level, husband's schooling and marital status. Results for each potential mediator which was separately associated with the outcome are presented in Table 9-14.

Of all the variables that were thought of as likely to act as mediators, assistance in housework, waist circumference, BMI, diabetes and to a lesser extend W/H ratio seem to exert enough change to be considered in this role. When the "assistance with housework" variable was introduced into the regression model, the regression coefficient of Triglycerides on parity decreased strongly from 0.036 to 0.025 mmol/L per each additional child, suggesting that the influence between parity and Triglyceride is mediated partially by assistance with housework.

The regression coefficient for assistance with housework was 0.31 mmol/L, suggesting an average increase of mean Triglycerides levels among those with assistance. When waist circumference and BMI were introduced into the model, each individually, the regression coefficient of Triglycerides on parity decreased from 0.036 to 0.025 and to 0.027 mmol/L respectively. With diabetes added to the model, the regression coefficient of Triglycerides on parity dropped from 0.036 to 0.028 mmol/L.

Other possible mediators made only small changes to the regression coefficient of parity, so their mediating effects were non-existence or slight. These were abdominal obesity (W/H ratio) and fasting insulin level as shown in Table 9-14.

Table 9-14: Effect of mediators along the causal pathway between parity and Triglycerides on the fully adjusted regression coefficient

Additional characteristics (mediators)	Slope (regression coefficient) for TG on parity	95% CI		P value	Slope (regression coefficient) of additional characteristic	95% CI		P value
		L	U			L	U	
Unadjusted	0.038	0.013	0.06	0.003				
Fully adjusted	0.036	0.003	0.068	0.033				
Assistance in house	0.025	-0.009	0.058	0.147	0.31	0.063	0.55	0.013
Diabetic	0.028	-0.003	0.059	0.078	0.87	0.61	1.13	<0.0001
Waist circumference	0.025	-0.008	0.057	0.137	0.61	0.32	0.91	<0.0001
W/H ratio	0.033	0.0003	0.066	0.047	0.28	0.08	0.49	0.008
BMI	0.027	-0.006	0.060	0.111	0.33	0.10	0.56	0.005
Insulin	0.035	0.001	0.066	0.041	0.015	-0.002	0.030	0.053

In summary, there was a definite association between Triglycerides and parity with both variables taken as continuous variables. Confounders could not explain this association. There seem to be a strong mediating effect of BMI, WC, assistance in housework and being diabetic, and with each of these included, the association between parity and Triglycerides became non significant.

9.7 T-CHOL/ HDL-C Ratio and Parity

Table 9-15 shows the relationship between raised T-CHOL/ HDL-C ratio and parity in groups. No significant association with parity was shown before or after adjustment.

Table 9-15: Unadjusted and adjusted odds ratios for the effect of grouped parity on raised T-CHOL/ HDL-C ratio > 0.13 mmol/L

Parity	n	%	Ratio of T-CHOL/ HDL-C > 0.13 mmol/L					
			Unadjusted			Adjusted		
			OR	95% CI				
				Lower	Upper	OR	Lower	Upper
0	40	25.0	0.49	0.22	1.07	0.28	0.07	1.06
1-3	33	24.2	0.47	0.20	1.11	0.57	0.22	1.48
4-6	111	35.1	0.80	0.479	1.32	0.97	0.55	1.70
7-9	161	33.5	0.74	0.468	1.17	0.79	0.48	1.28
10+	153	40.5	1			1		
P-value					0.235			0.287

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable and T-Chol/ HDL-C level was kept as a categorical variable as in Table 9-14, an apparent association between T-CHOL/ HDL-C ratio and parity was observed. The unadjusted change in odds of T-CHOL/ HDL-C > 0.13 mmol/L per extra child (unit change in parity) was 1.06 (95% CI 1.00 to 1.11, p=0.039), an evidence of an association between parity and triglycerides in unadjusted analysis. This association was completely abolished after adjustment for age, women's educational level, husband's years of schooling and marital status as in Table 9-16.

Table 9-16: The change of unadjusted and adjusted odds of T-CHOL/ HDL-C ratio > 0.13 mmol/L per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.06	0.03	1.00	1.11	0.039
Adjusted for age, educational level, husband's years of schooling and marital status	1.04	0.03	0.98	1.11	0.168

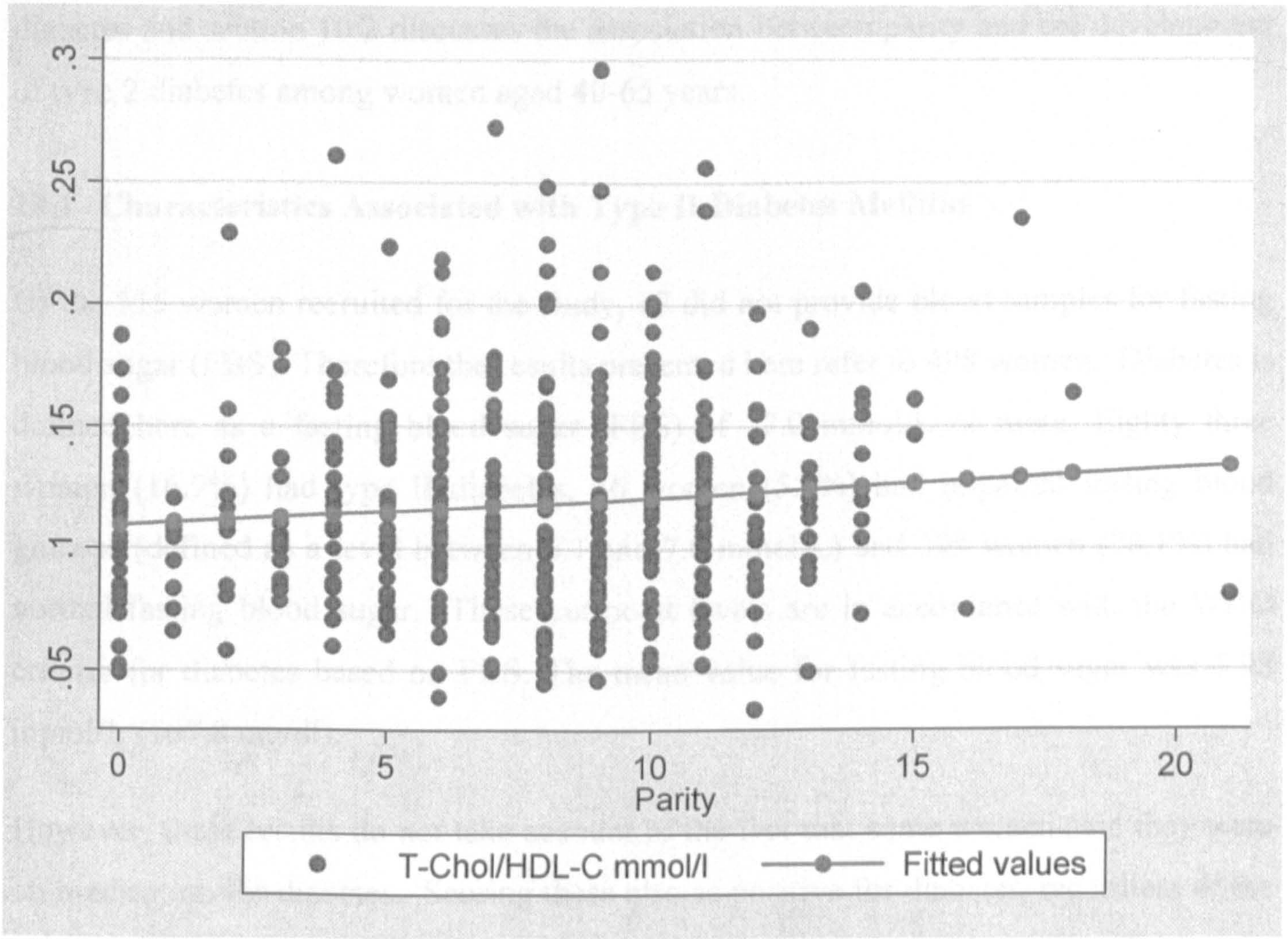
With both variables, parity and T-CHOL/ HDL-C ratio, on continuous scales, using ordinary regression, the mean T-CHOL/ HDL-C increased by 0.001 mmol/L per extra child, p= 0.020. But this association was attenuated after adjustment for age, and was completely abolished after adjustment for women's educational level, husband's years of schooling and marital status as in Table 9-17.

Table 9-17: The Unadjusted and Adjusted Regression Slopes of T-CHOL/ HDL-C Ratio on Parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.001	0.0005	0.0003	0.002	0.020
Adjusted for age, educational level, husband's years of schooling and marital status	0.0008	0.0005	0.0006	0.002	0.282

Figure 9-5 shows the scatter plot of the two variables T-CHOL/ HDL-C and parity with the regression line.

Figure 9-5: Scatter Plot of T-CHOL/ HDL-C and parity



There was an association between gravidity and T-CHOL/ HDL-C ratio when T-CHOL/ HDL-C ratio was regressed on gravidity. This association was attenuated when adjusted for age.

In the absence of a statistical association in the above adjusted analysis, analysis of mediators is not presented.

Chapter 10
PARITY AND THE DEVELOPMENT OF TYPE II DIABETES MELLITUS

Does parity contribute to the development of type II diabetes in women? Does the association between parity and type II diabetes exists independently or is it confounded by socio-economic status, or mediated by behavioural factors and / or obesity?

Results on the association between parity and type II diabetes mellitus are presented in this chapter. Section 10.1 focuses on the general characteristics associated with type II diabetes and section 10.2 discusses the association between parity and the development of type 2 diabetes among women aged 40-65 years.

10.1 Characteristics Associated with Type II Diabetes Mellitus

Of the 515 women recruited for the study, 17 did not provide blood samples for fasting blood sugar (FBS). Therefore the results presented here refer to 498 women. Diabetes is defined here as a fasting blood sugar (FBS) of 7.0 mmol/L or more. Eighty three women (16.7%) had type II diabetes, 26 women (5.2%) had impaired fasting blood glucose (defined as a level between 6.1 and 7.0 mmol/L) and 398 women (78.1%) had normal fasting blood sugar. These cut-point levels are in accordance with the WHO criteria for diabetes based on FBS. The mean value for fasting blood sugar was 5.98 mmol/L (107.8 mg/dl).

However, these results do not take account of the fact that some women said they were on medication for diabetes. Scoring these also as positive for diabetes, regardless of the measured FBS, changes the number of women with diabetes to 115, 22.3%. Taking the FBS level for these women as "at least" as measured, a censored regression model for the mean allowing for censoring (see above) was 6.3 mmol/L among the 498 women.

Characteristics associated with diabetes are shown in Table 10-1. A higher risk of diabetes among women was observed with increasing age, and menopausal status. Both WC and W/H ratio were positively and significantly associated with diabetes while BMI was not. Women with diabetes had elevated cholesterol, elevated LDL-C, elevated triglycerides, elevated T-CHOL/HDL-C levels and had a decreased level of HDL-C. Family history of diabetes was positively associated with type II diabetes. Diabetic women have elevated DBP, SBP and hypertension compared to non-diabetic women in

the survey. Type II diabetes was more prevalent among the less educated and the physically inactive, widowed and married women, but the association did not reach the significant level.

Table 10-1: Characteristics associated with Diabetes (Fasting Blood Sugar)

	Number of women	Diabetic ≥ 7.0 mmol/L/ medication n	%	Statistical significance P- value
Demographic and socio-economic variables				
Age in years				**< 0.0001**
< 45	159	(19)	12.0	
45-49	115	(20)	17.4	
50-54	110	(31)	28.2	
55-59	95	(32)	33.7	
60+	35	(13)	37.1	
Years of schooling				0.076
No formal education	119	(32)	26.9	
Elementary	199	(51)	25.6	
Secondary	167	(27)	16.2	
Higher	30	(5)	16.7	
Current employment				0.438
No	436	(100)	22.9	
Yes	79	(15)	19.0	
Women's Occupation				0.536
Unskilled worker	16	(3)	18.8	
Skilled worker	14	(2)	14.3	
Employee	24	(3)	12.5	
Private business	25	(7)	28.0	
Marital status				0.370
Single	21	(4)	19.1	
Married	382	(83)	21.7	
Divorced/separated	28	(4)	14.3	
Widowed	84	(24)	28.6	
Husband's years of schooling				0.241
No formal education	85	(25)	29.4	
Elementary	166	(41)	24.7	
Secondary	170	(34)	20.0	
Higher	58	(10)	17.2	
Husband's currently employed				0.082
No	141	(39)	27.7	
Not applicable	112	(28)	25.0	
Yes	241	(44)	18.3	
Own automatic washing machine				0.272
No	400	(85)	21.3	
Yes	115	(30)	26.1	

	Number of women	Diabetic ≥ 7.0 mmol/L/ medication n	%	Statistical significance P- value
Family affluence scale				0.209
Poor	225	(42)	18.7	
Average	164	(42)	25.6	
Better off	126	(31)	24.6	
Behavioural risk factors				
Physical activity				0.286
No	445	(103	23.2	
Yes	69	(12)	17.4	
Smoking habits				0.689
Never smoked	481	(108)	22.5	
Current smoker	28	(5)	17.9	
Ex-smoker	6	(2)	33.3	
Watch TV				0.906
No	31	(7)	22.6	
Yes	484	(108)	22.3	
Hours/week watch TV				0.603
< = 4 hours	24	(7)	29.2	
5- 10 hours	150	(36)	24.0	
11- 20 hours	133	(25)	18.8	
21+ hours	177	(40)	22.6	
Assistance in house-work				0.174
No	142	(31)	21.8	
Yes	372	(83)	22.3	
Stress level				0.710
No	154	(36)	23.4	
Yes	361	(79)	21.9	
Reproductive health variables				
Parity				0.749
0	42	(9)	21.4	
1-3	38	(6)	15.8	
4-6	117	(25)	21.4	
7-9	165	(36)	21.8	
10+	153	(39)	25.5	
Age at 1st marriage				0.686
<18	232	(54)	23.3	
18+	262	(57)	21.8	
Age at 1st birth				0.224
≤ 18	173	(44)	25.4	
> 18	301	(62)	20.6	
Gravidity				0.638
0	38	(8)	21.1	
1- 3	33	(5)	15.2	
4- 6	65	(13)	20.0	
7- 9	136	(28)	20.6	
10+	243	(61)	25.1	

	Number of women	Diabetic ≥ 7.0 mmol/L/ medication n	%	Statistical significance P- value
Age at menarche				0.091
< = 11	39	(8)	20.5	
12	108	(32)	29.6	
13	138	(32)	23.2	
14	133	(27)	20.3	
15+	90	(12)	13.3	
History of infertility				0.704
No	441	(98)	22.2	
Yes	53	(13)	24.5	
Pregnancy ended as abortion or miscarriage				0.268
No	164	(32)	19.5	
Yes	313	(75)	24.0	
Pregnancy ended as a stillbirth				0.274
No	412	(89)	21.6	
Yes	65	(18)	27.7	
Have you ever had polycystic ovaries				0.369
No	495	(114)	23.0	
Yes	13	(1)	7.7	
Have your periods stopped now				**<0.0001**
No	285	(46)	16.1	
Yes	229	(68)	29.7	
Age at menopause				**0.011**
<= 44	44	(7)	15.9	
45- 49	75	(18)	24.0	
50- 54	95	(39)	41.1	
55+	15	(4)	26.7	
Ever use C P				0.336
No	306	(64)	20.9	
Yes	208	(51)	24.5	
Serological variables				
T-Cholesterol				**0.016**
Normal	377	(65)	17.3	
Elevated T-Chol	121	(33)	27.3	
LDL-Cholesterol				**0.001**
Normal	399	(67)	16.8	
Elevated LDL_C	99	(31)	31.3	
HDL-Cholesterol				**0.003**
Decreased HDL	247	(62)	25.1	
Normal	251	(36)	14.3	

	Number of women	Diabetic ≥ 7.0 mmol/L/ medication n	%	Statistical significance P- value
Triglyceride level				**<0.0001**
Normal	343	(42)	12.2	
Elevated	155	(56)	36.1	
Ratio of T-chol/HDL-Chol				**< 0.0001**
Normal	325	(47)	14.5	
High risk	173	(51)	29.5	
Hypertensive				**<0.0001**
No	295	(45)	15.3	
Yes	220	(70)	31.8	
Diastolic BP				**0.002**
Normal	332	(60)	18.1	
Elevated ≥90 mmHg or on medication	183	(55)	30.1	
Systolic BP				**< 0.0001**
Normal	318	(46)	14.5	
Elevated ≥140 mmHg or on medication	197	(69)	35.0	
Central obesity, waist circum ≥ 88 cm				**0.004**
Normal	81	(8)	9.9	
WC ≥ 88 cm	432	(106)	24.5	
BMI				0.102
Non-obese	158	(28)	17.7	
Obese BMI ≥30kg/m2	355	(86)	24.2	
Abdominal obesity, W/H ratio ≥ 0.85 cm				**<0.0001**
Normal	247	(29)	11.7	
WHR ≥ 0.85	266	(85)	32.0	
Family History of diabetes				**0.009**
No	301	(55)	18.3	
Yes	214	(60)	28.0	

Table 10-1 shows associations of diabetes with various categorical variables. Table 10-2 shows the means of continuous variables in the groups with and without type II diabetes mellitus. Women with type II diabetes were significantly older and with less years of education than women with normal glucose tolerance. BMI was not significantly different between the two groups of women, which was not the case with central obesity measured by waist circumference and abdominal obesity measured by W/H ratio. Women who were diabetic had higher WC and higher W/H ratio compared to women with normal glucose tolerance. Women with type II diabetes had a significantly higher systolic BP, and hypertension compared to women with normal glucose tolerance.

Diabetic women reported significantly more pregnancies on average, with an excess of 1.2 pregnancies. The excess in number of children 0.6 was much less, and not statistically significant.

Of the blood lipids, Triglycerides were significantly higher in women with type II diabetes than those with normal glucose tolerance. Women with normal glucose tolerance had lower total cholesterol, LDL-C and T-CHOL/DHL-C ratio but a higher HDL-C than women with type II diabetes. Moreover, women with type II diabetes were significantly more likely than normoglycemic to have a family history of diabetes.

Table 10-2: Mean values of selected characteristics associated with diabetic status among Palestinian Women

Characteristic	Normal glucose tolerance (NGT)		Diabetes Mellitus (DM)		P value
	(N)	Mean ± SD	(N)	Mean ± SD	
Age (years)	(399)	48.6 ± 6.3	(115)	52.0 ± 6.2*	<0.0001
Education (years)	(400)	5.9 ± 4.3	(115)	4.7 ± 4.1	0.0108
Body Mass Index (BMI)	(399)	33.0 ± 6.0	(115)	34.0 ± 5.9	0.1390
Waist circumference	(399)	97.0 ± 12.3	(115)	101.8 ± 10.2	< 0.0001
W/H ratio	(399)	0.84 ± .07	(115)	0.88 ± .05	< 0.0001
Systolic BP (mm Hg) (1)	(399)	128.4 ± 22.9	(115)	140.4 ± 23.2	< 0.0001
Diastolic BP (mm Hg) (1)	(399)	81.6 ± 11.3	(115)	83.6 ± 12.1	0.0962
Triglycerides (mmol/L)	(400)	1.42 ± .96	(98)	2.2 ± 1.26	< 0.0001
Total Cholesterol (mmol/L)	(400)	4.51 ± 1.1	(98)	5.0 ± 1.13	< 0.0001
LDL-C (mmol/L)	(400)	2.67 ± 1.01	(98)	3.11 ± 1.09	0.0002
HDL-C (mmol/L)	(400)	1.09 ± .29	(98)	0 .99 ± .26	0.0018
Total CHOL/HDL-C ratio	(400)	0 .11± .04	(98)	0 .14± .04	< 0.0001
Number of pregnancies	(400)	8.6 ± 4.4	(115)	9.8 ± 4.9	0.0134
Number of children	(400)	7.2 ± 3.6	(115)	7.8 ± 3.8	0.1077

(1) Adjusted for censoring among those on medication for hypertension

10.2 Further Analysis of Parity and the Development of Type II Diabetes Mellitus

In the following section, we aim to test the hypothesis that an increasing number of children was associated with an increasing risk of developing type II diabetes among these older Palestinian women living in refugee camps. The initial results were shown in sections 7.6, 7.7 and 10.1 but this section takes further the relationship of parity and the risk of developing type II diabetes mellitus. This association was assessed using the same statistical models as in parity and lipids.

The effect of grouped parity on type II diabetes (defined as raised fasting blood sugar and/or on medication) was assessed in models controlling for age, women's education, husband's years of schooling and marital status and as seen in Table 10-3. The unadjusted and adjusted models show no overall statistically significant association, p=0.753 and p=0.763 respectively.

Table 10-3: Unadjusted and adjusted odds ratios for the effect of parity in groups on Diabetes (raised FBS ≥ 7.00 mmol/L or on medication)

Parity	n	%	Raised fasting Blood Sugar (FBS) or medication					
			Unadjusted			Adjusted		
			OR	95% CI		OR	Lower	Upper
				Lower	Upper			
0	42	21.4	0.80	0.35	1.81	1.12	0.35	3.58
1-3	38	15.8	0.55	0.21	1.41	0.51	0.17	1.55
4-6	117	21.4	0.79	0.45	1.41	1.08	0.57	2.04
7-9	165	21.8	0.81	0.49	1.37	1.01	0.58	1.76
10+	153	25.5	1			1		
P-value					0.753			0.763

Adjustment for age, woman's education, husband's education, and marital status

In the next two statistical models, the association between parity and fasting blood sugar was assessed with parity measured on a continuous scale using ordinary regression with FBS introduced into the regression model as both categorical and as a continuous variable as in Tables 10-4 and 10-5. When parity as a continuous variable and FBS kept as a categorical variable, an apparent non-significant association between parity and diabetes was observed in the unadjusted analysis. The change in unadjusted odds of FBS ≥ 7.00 mmol/L (diabetic) per extra child (unit change in parity) was 1.05 (95% CI 0.99 to 1.11, p= 0.108).

Table 10-4: The change of unadjusted and adjusted odds of increased diabetes per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.05	0.03	0.99	1.11	0.108
Adjusted for age, educational level, husband's years of schooling and marital status	1.02	0.04	0.97	1.1	0.492

Adjustment for age, women's educational level, husband's years of schooling and marital status, did not make noticeable difference to the association and it was insignificant as seen in Table 10-4.

The relationship was next examined with both variables being continuous, using censored ordinary regression, and by a scatter diagram as in Table 10-5 and Figure 10-1. The scatter diagram does not allow for censoring for those on medication, but nevertheless does give a useful picture. The unadjusted regression slope was 0.13 mmol/L, denoting the predicted rise in fasting blood sugar for a unit rise in parity, (95% CI: 0.04 to 0.22, p=0.004).

Table 10-5: The Unadjusted and Adjusted Regression Slopes of censored FBS mmol/L on Parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.13	0.05	0.04	0.22	0.004
Adjusted for age	0.09	0.05	-0.0004	0.18	0.051
Adjusted for age, educational level, husband's years of schooling and marital status	0.10	0.06	-0.02	0.21	0.092

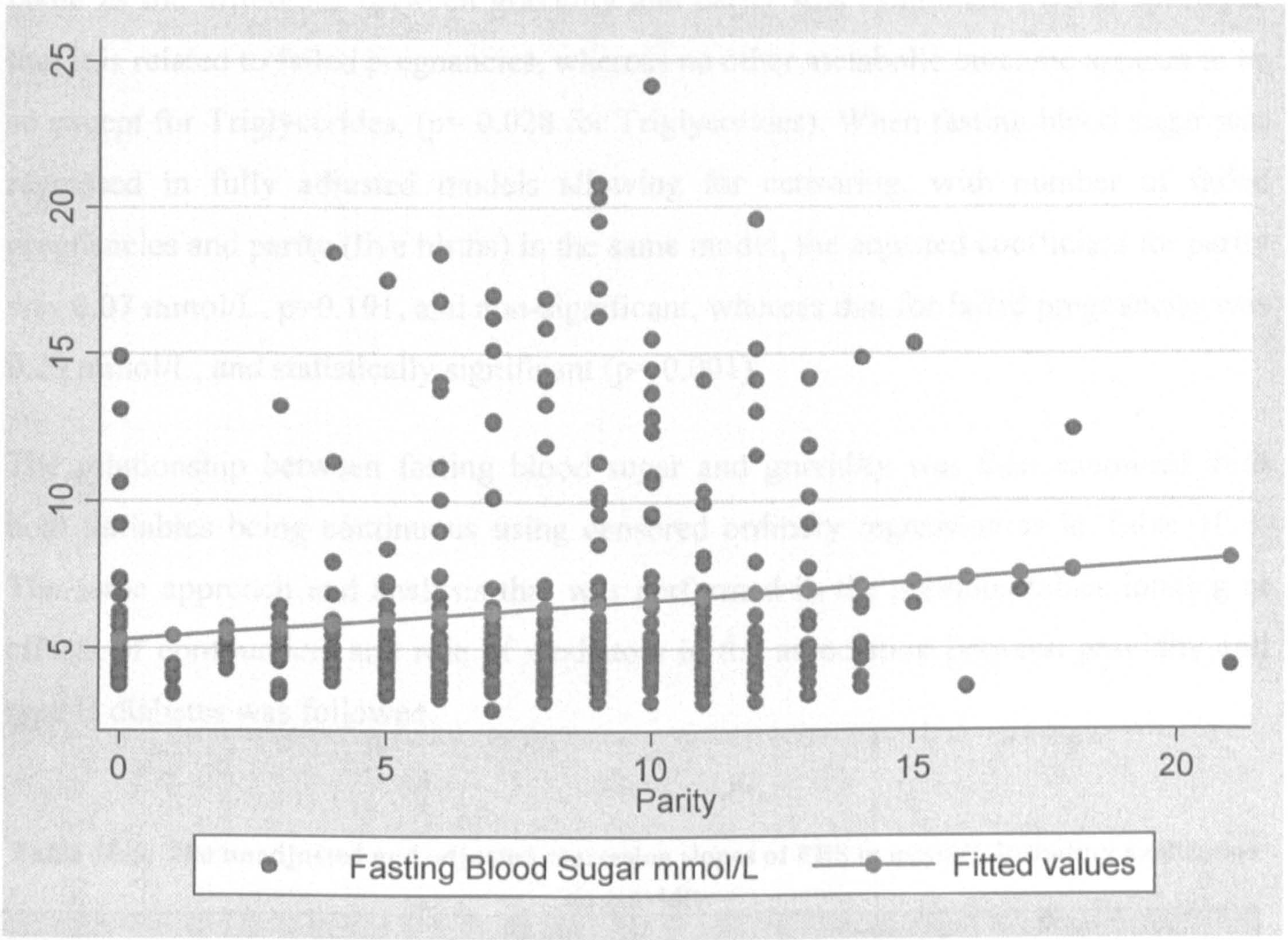
When adjusted for age, the slope was reduced and the significance of the association just disappeared. The adjusted mean increase in censored FBS per additional child was 0.09 mmol/L, (95% CI -0.0004 to 0.18, p= 0.051). Adjustment for the other confounders did not change the magnitude of the association but it became less significant. Since this left us with no evidence of an association between parity and the development of type II diabetes mellitus or with fasting blood sugar, investigating the effect of mediators was disregarded.

We also carried out a separate analysis to see if the mean FBS differed among those who reported having diabetes, between those taking medication and those not. Results indicated higher FBS among those who reported they were taking the medication compared to those who did not. These results suggest that, although women reported they were meant to be taking these drugs, adherence may have been patchy at best.

When FBS was regressed on gravidity, the regression coefficient of censored FBS increased by 0.015 mmol/L per extra child, (95% CI: 0.08 to 0.22, p<0.0001). Adjustment for confounders did not change the magnitude of the association, and it remained significant, while with parity the association disappeared after adjustment, as shown above. This led to taking the analysis further as detailed in section 10.3.

Figure 10-1 shows the scatter plot of the two variables FBS and parity with the regression line and suggests strongly that the linear model is adequate.

Figure 10-1: Scatter Plot of Fasting Blood Sugar (FBS) and parity



10.3 Justification for Taking Gravidity Rather than Parity in the Case of Fasting Blood Sugar and Diabetes

The analysis of fasting blood sugar and diabetes with parity did not suggest any evidence of association. However, one observes in Table 10-2 that there appears to be an association with gravidity. This contrast between parity and gravidity was not shown for the other metabolic outcome measurements, total cholesterol, LDL-C, HDL-C, and total cholesterol/HDL-C ratio, which did not show a significant association with either parity or gravidity. Triglyceride was the exception as it showed an association with gravidity as well as with parity. When medication was included in the definition of diabetes, the analysis suggested no significance association between (binary) diabetes and gravidity. However in censored regression analysis, a significant association was observed between diabetes and gravidity.

Purely speculatively, given that the decision to do this was made after the previous analysis, this relationship was pursued further.

As a preliminary to this, the association of FBS with number of failed pregnancies, taken as the difference between gravidity and parity was examined. FBS is special in that it is related to failed pregnancies, whereas no other metabolic outcome appears to be so except for Triglycerides, (p= 0.028 for Triglycerides). When fasting blood sugar was regressed in fully adjusted models allowing for censoring, with number of failed pregnancies and parity (live births) in the same model, the adjusted coefficient for parity was 0.07 mmol/L, p=0.191, and non-significant, whereas that for failed pregnancies was 0.29 mmol/L, and statistically significant (p= 0.001).

The relationship between fasting blood sugar and gravidity was then examined with both variables being continuous using censored ordinary regression as in Table 10-6. The same approach and analysis that was performed in the previous tables looking at effects of confounders and role of mediators in the association between gravidity and type II diabetes was followed.

Table 10-6: The unadjusted and adjusted regression slopes of FBS in mmol/L including medication on gravidity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.15	0.04	0.08	0.22	<0.0001
Adjusted for age, educational level, husband's years of schooling and marital status	0.14	0.05	0.05	0.23	0.002

The unadjusted regression slope was 0.15 mmol/L, denoting the predicted rise in fasting blood sugar for a unit rise in gravidity, (95% CI: 0.08 to 0.22, p <0.0001). Adjustment for age, women's education, husband's education and marital status reduced slightly the magnitude of the association but it remained significant. So confounders could not explain the association between gravidity and type II diabetes.

10.4 Other Characteristics and Mediators

Results for the role of mediators and other correlates are shown in Table 10-7. In these regression models, all variables that were significantly associated with type II diabetes were introduced to test their roles individually and to test if they act as mediators in the relationship between gravidity and diabetes.

Table 10-7: Effect of mediators along the causal pathway between gravidity (number of pregnancies) and diabetes (FBSmmol/L) with medication on the fully adjusted regression coefficient

Additional characteristics (mediators)	Slope (regression coefficient) for FBS on parity	95% CI		P value	Slope (regression coefficient) of additional characteristi	95% CI		P value
		L	U			L	U	
Unadjusted	0.15	0.08	0.22	<0.0001				
Fully adjusted	0.14	0.05	0.23	0.002				
F H of diabetes	0.13	0.05	0.22	0.003	1.33	0.63	2.0	<0.0001
Age at menarche	0.14	0.05	0.23	0.003	-0.26	-0.51	-.02	0.038
Failed pregnancy	0.07	-0.04	0.19	0.191	0.21	-0.005	0.43	0.055
Central obesity WC	0.12	0.03	0.22	0.007	0.04	0.007	0.07	0.015
Abdominal obesity W/H ratio	0.13	0.04	0.22	0.005	12.39	7.01	17.8	<0.0001

Failed pregnancies (the difference between gravidity and parity) seem to have the highest mediating effect amongst all mediating variables since it has reduced the magnitude of the association to a great extent. This is to be expected as failed pregnancies is the component of gravidity that predicts FBS The result here confirms that association between gravidity and type II diabetes goes through failed pregnancies.

On the other hand, WC and W/H ratio have slightly reduced the magnitude of the association between gravidity and type II diabetes as well, which indicates a partial mediating effect for WC and W/H ratio.

Chapter 11
PARITY, DIASTOLIC, SYSTOLIC BLOOD PRESSURE AND HYPERTENSION

This chapter examines the relationships among parity, systolic blood pressure (SBP), diastolic blood pressure (DBP) and hypertension, investigating the independent relation of the number of children to blood pressure and hypertension. Section 11.1 focuses on the general characteristics associated with elevated systolic, diastolic blood pressure and hypertension. Sections 11.2 and 11.3 explore whether increasing parity leads to a subsequent elevation of diastolic and systolic blood pressure in these women.

11.1 Characteristics Associated with Elevated SBP, DBP and Hypertension

Results presented in the analysis of blood pressure refer to 513 women out of the 515 women recruited for the study, two records containing information on SBP and DBP not being available. Systolic blood pressure ranged from 78 mmHg to 221 mmHg, with a mean of 131 mmHg. Diastolic blood pressure ranged from 53 mmHg to 123.5 mmHg, with a mean of 82 mmHg. On the basis of these measurements 434 women were classified as normotensive and 81 women (15.7%) as hypertensive. After the inclusion of antihypertensive medication in the definition, 295 women were classified as normotensive and 220 women (42.7%) as hypertensive, and the mean SBP and DBP with correction for censoring among those on medication became 135 mmHg and 84 mmHg respectively. The characteristics associated with elevated SBP, DBP and hypertension is shown in Table 11-1.

Women with elevated SBP, DBP and hypertension were significantly older, more often widowed, less educated, and physically less active with more central and abdominal obesity and more frequently menopausal. They had elevated total cholesterol, elevated triglycerides and were more frequently diabetic. Women with elevated systolic blood pressure tended to be also more obese, diabetic with higher levels of total cholesterol and LDL-C. They tended to have more pregnancies that ended as still births and were less educated. It is interesting to notice that neither parity nor gravidity has a significant association with elevated SBP and DBP.

Table 11-1: Characteristics associated with potential risk factors SBP ≥ 140 mmHg or on medication, DBP≥ 90 mmHg or on medication, hypertension ≥ 140/90 mmHg or on medication

Characteristic	No of women	SBP ≥ 140 mmHg or on medication (n) %	P	DBP≥ 90 mmHg or on medication (n) %	P	Blood pressure ≥ 140/90 mmHg or on medication (n) %	P
Demographic and socio-economic variables							
Age			**<0.0001**		**<0.0001**	**corrected**	**<0.0001**
<45	159	(28) 17.6		(31) 19.5		(34) 21.4	
45-49	115	(42) 36.5		(37) 32.2		(47) 40.9	
50.54	110	(54) 49.1		(47) 42.7		(60) 54.6	
55-59	95	(50) 52.6		(47) 49.5		(54) 56.8	
60+	35	(23) 65.7		(21) 60.0		(25) 71.4	
Women's education			**<0.0001**		**<0.0001**		**<0.0001**
No formal education	119	(55) 46.2		(49) 41.2		(60) 50.4	
Elementary	199	(93) 46.7		(87) 43.7		(101) 50.8	
Secondary	167	(44) 26.4		(42) 25.2		(53) 31.7	
Higher education	30	(5) 16.7		(5) 16.7		(6) 20.0	
Marital status			**0.008**		**<0.0001**		**<0.0001**
Married	382	(135) 35.3		(123) 32.2		(149) 39.0	
Single	21	(7) 33.3		(6) 28.6		(7) 33.3	
Divorced/separated	28	(9) 32.1		(7) 25.0		(10) 35.7	
widowed	84	(46) 54.8		(47) 56.0		(54) 64.3	
Currently employed			0.288		0.121		0.241
No	436	(171) 39.2		(161) 36.9		(191) 43.8	
Yes	79	(26) 32.9		(22) 27.9		(29) 36.7	
Occupation			0.065		0.106		0.144
Unskilled worker	16	(8) 50.0		(5) 31.3		(8) 50.0	
Skilled worker	14	(3) 21.4		(2) 14.3		(3) 21.4	
Employee	24	(4) 16.7		(4) 16.7		(6) 25.0	
Private business	25	(11) 44.0		(11) 44.0		(12) 48.0	

Characteristic	No of women	SBP ≥ 140 mmHg or on medication (n) %	P	DBP≥ 90 mmHg or on medication (n) %	P	Blood pressure ≥ 140/90 mmHg or on medication (n) %	P
Husband's education			**0.006**		**0.033**		**0.009**
No formal education	85	(38) 44.7		(32) 37.7		(40) 47.1	
Elementary	166	(77) 46.4		(72) 43.4		(86) 51.8	
Secondary	170	(51) 30.0		(48) 28.2		(58) 34.1	
Higher education	58	(18) 31.0		(19) 32.8		(23) 39.7	
Husband currently employed			**0.028**		**0.004**		**0.002**
Yes	241	(83) 34.4		(72) 29.9		(91) 37.8	
No	141	(52) 36.9		(51) 36.2		(58) 41.1	
Not applicable	112	(55) 49.1		(54) 48.2		(64) 57.1	
Own automatic washing machine			0.826		0.802		0.407
No	400	(152) 38.0		(141) 35.3		(167) 41.8	
Yes	115	(45) 39.1		(42) 36.5		(53) 46.1	
Family affluence scale			0.183		0.083		**0.047**
Poor	225	(76) 33.8		(68) 30.2		(84) 37.3	
Average	164	(68) 41.5		(64) 39.0		(72) 43.9	
Better off	126	(53) 42.1		(51) 40.5		(64) 50.8	
Behavioural risk factors							
Physical activity			**<0.0001**		**<0.0001**		**<0.0001**
No	446	(185) 41.6		(173) 38.9		(206) 46.3	
Yes	69	(12) 17.4		(10) 14.5		(14) 20.3	
Smoking habits			0.830		0.724		0.858
Never smoked	481	(183) 38.1		(173) 36.0		(204) 42.4	
Ex-smoker	28	(11) 39.3		(8) 28.6		(13) 46.4	
Current smoker	6	(3) 50.0		(2) 33.3		(3) 50.0	
Watch TV			0.663		0.703		0.777

Characteristic	No of women	SBP ≥ 140 mmHg or on medication (n) %	P	DBP≥ 90 mmHg or on medication (n) %	P	Blood pressure ≥ 140/90 mmHg or on medication (n) %	P
No	31	(13) 41.9		(12) 38.7		(14) 45.2	
Yes	484	(184) 38.0		(171) 35.3		(206) 42.6	
Hours/week watch TV			**0.027**		0.111		0.201
≤ 4	24	(14) 58.3		(13) 54.2		(14) 58.3	
5-10	150	(45) 30.0		(48) 32.0		(56) 37.3	
11-20	133	(52) 39.1		(42) 31.6		(56) 42.1	
21+	177	(73) 41.2		(68) 38.4		(80) 45.2	
Assistance in house-work			0.113		0.094		0.167
No	142	(46) 32.4		(42) 29.6		(53) 37.3	
Yes	372	(150) 40.3		(140) 37.6		(166) 44.6	
Stress level			0.160		0.207		0.310
No	154	(66) 42.9		(61) 39.6		(71) 46.1	
Yes	361	(131) 36.3		(122) 33.8		(149) 41.3	
Reproductive Health Factors							
Parity			0.231		0.849		0.382
0	42	(11) 26.2		(12) 28.6		(13) 31.0	
1-3	38	(13) 34.2		(14) 36.8		(14) 36.8	
4-6	117	(40) 34.2		(42) 35.9		(49) 41.9	
7-9	165	(67) 40.6		(57) 34.6		(72) 43.6	
10+	153	(66) 43.1		(58) 37.9		(72) 47.1	
Age at 1st marriage, yrs			0.332		0.057		0.272
<18	232	(84) 36.2		(73) 31.5		(94) 40.5	
18+	262	(106) 40.5		(104) 39.7		(119) 45.4	
Age at 1st birth			0.982		0.935		0.780

Characteristic	No of women	SBP ≥ 140 mmHg or on medication (n) %	P	DBP≥ 90 mmHg or on medication (n) %	P	Blood pressure ≥ 140/90 mmHg or on medication (n) %	P
≤ 18	173	(68) 39.3		(62) 35.8		(77) 44.5	
> 18	301	(118) 39.2		(109) 36.2		(130) 43.2	
Gravidity			0.061		0.364		0.155
0	38	(11) 29.0		(12) 31.6		(13) 34.2	
1- 3	33	(12) 36.4		(12) 36.4		(13) 39.4	
4- 6	65	(20) 30.8		(21) 32.3		(25) 38.5	
7- 9	136	(45) 33.1		(41) 30.2		(51) 37.5	
10+	243	(109) 44.9		(97) 39.9		(118) 48.6	
Age at menarche			0.147		0.125		**0.039**
≤ 11	39	(17) 43.6		(18) 46.2		(22) 56.4	
12	108	(50) 46.3		(46) 42.6		(53) 49.1	
13	138	(52) 37.7		(49) 35.5		(61) 44.2	
14	133	(50) 37.6		(43) 32.3		(54) 40.6	
15+	90	(26) 28.9		(25) 27.8		(28) 31.1	
History of infertility			0.679		0.759		0.965
No	441	(171) 38.8		(157) 35.6		(190) 43.1	
Yes	53	(19) 35.9		(20) 37.7		(23) 43.4	
Pregnancy ended as abortion or miscarriage			0.116		0.172		0.163
No	164	(56) 34.2		(52) 31.7		(64) 39.0	
Yes	313	(130) 41.5		(119) 36.0		(143) 45.7	
Pregnancy ended as a stillbirth			**0.036**		0.062		0.067
No	412	(153) 37.1		(141) 34.2		(172) 41.8	
Yes	65	(33) 50.8		(30) 46.2		(35) 53.9	
Have you ever had polycystic ovaries			0.622		0.740		0.667

Characteristic	No of women	SBP ≥ 140 mmHg or on medication (n) %	P	DBP≥ 90 mmHg or on medication (n) %	P	Blood pressure ≥ 140/90 mmHg or on medication (n) %	P
No	495	(191) 38.6		(175) 35.6		(211) 42.6	
Yes	13	(4) 30.8		(5) 38.5		(6) 46.2	
Ever use CP			0.751		0.566		0.720
No	306	(119) 38.9		(112) 36.6		(129) 42.2	
Yes	208	(78) 37.5		(71) 34.1		(91) 43.8	
Have your periods stopped now			**<0.0001**		**<0.0001**		**<0.0001**
No	285	(81) 28.4		(75) 26.3		(92) 32.3	
Yes	229	(116) 50.7		(108) 47.2		(128) 55.9	
Age at menopause in years			0.746		0.942		0.975
≤ 44	44	(19) 43.2		(21) 47.7		(24) 54.6	
45-49	75	(39) 52.0		(36) 48.0		(41) 54.7	
50-54	95	(50) 52.6		(43) 45.3		(54) 56.8	
55+	15	(8) 53.3		(8) 53.3		(9) 60.0	
Ever used HRT			0.150		**0.014**		**0.043**
No	509	(193) 37.9		(178) 35.0		(215) 42.2	
Yes	6	(4) 66.7		(5) 83.3		(5) 83.3	
Metabolic risk factors							
Cholesterol (mmol/L)			**0.001**		**0.050**		**0.003**
Normal	377	(129) 34.1		(125) 33.2		(147) 39.0	
Elevated cholesterol	121	(61) 50.4		(52) 43.0		(66) 54.6	
LDL-Cholesterol (mmol/L)			**0.009**		0.067		**0.016**
Normal	399	(141) 35.3		(134) 33.6		(160) 40.1	
Elevated LDL-chol	99	(49) 49.5		(43) 43.4		(53) 53.5	
HDL-Cholesterol (mmol/L)			0.745		0.124		0.670
Decreased HDL-Chol	247	(96) 38.9		(96) 38.9		(108) 43.7	

Characteristic	No of women	SBP ≥ 140 mmHg or on medication (n) %	P	DBP≥ 90 mmHg or on medication (n) %	P	Blood pressure ≥ 140/90 mmHg or on medication (n) %	P
Normal	251	(94) 37.5		(81) 32.3		(105) 41.8	
Triglyceride (mmol/L)			**0.030**		**0.027**		**0.036**
Normal	343	(120) 35.0		(111) 32.4		(136) 39.7	
Elevated TG	155	(70) 45.2		(66) 42.6		(77) 49.7	
TChol / LDH-chol			0.999		0.920		0.850
Normal	325	(124) 38.2		(115) 35.4		(140) 43.1	
High risk	173	(66) 38.2		(62) 35.8		(73) 42.2	
Diabetic, % ≥7.00 mmol/L or on medication			**<0.0001**		**0.002**		**<0.0001**
No	400	(128) 32.0		(128) 32.0		(150) 37.5	
Yes	115	(69) 60.0		(55) 47.8		(70) 60.9	
Anthropometric factors							
Central obesity, waist circum ≥ 88 cm			**<0.0001**		**<0.0001**		**<0.0001**
Normal	81	(12) 14.8		(10) 12.4		(14) 17.3	
WC ≥ 88 cm	432	(183) 42.4		(171) 39.6		(204) 47.2	
BMI			***0.002***		**0.001**		**<0.0001**
Non-obese	158	(44) 27.9		(39) 24.7		(49) 31.0	
Obese BMI ≥30kg/m^2	355	(151) 42.5		(142) 40.0		(169) 47.6	
Abdominal obesity, W/H ratio ≥ 0.85 cm			**<0.0001**		**<0.0001**		**<0.0001**
Normal	247	(68) 27.5		(66) 26.7		(82) 33.2	
WHR ≥ 0.85	266	(127) 47.7		(115) 43.2		(136) 51.1	
Self rating of obesity			**0.001**		**<0.0001**		***0.002***
Underweight	21	(7) 33.3		(7) 33.3		(7) 33.3	
Normal weight	141	(43) 30.5		(41) 29.1		(51) 36.2	
Overweight	228	(80) 35.1		(70) 30.7		(91) 39.9	

Characteristic	No of women	SBP ≥ 140 mmHg or on medication (n) %	P	DBP≥ 90 mmHg or on medication (n) %	P	Blood pressure ≥ 140/90 mmHg or on medication (n) %	P
Obese	94	(49) 52.1		(46) 48.9		(51) 54.3	
Very obese	26	(16) 61.5		(17) 65.4		(18) 69.2	

11.2 Further Analysis of Systolic Blood Pressure (SBP) and Parity

In this section, we aim to test the hypothesis that an increasing number of children is associated with an elevation of systolic blood pressure. The initial results concerning parity and then women's principal characteristics were shown in sections 7.6 and 7.7 and this section takes the relationship between parity and SBP further. Table 11-2 shows the unadjusted and adjusted effect of parity on the categorisation of raised SBP ≥ 140 mmHg or on medication, with no significant association seen in the unadjusted odds ratios. Before and after adjustment for confounders (age, women's education, husband's years of schooling and marital status), the association remained non-significant, p= 0.238 and p= 0.126 respectively.

Table 11-2: Unadjusted and adjusted odds ratios for the effect of parity in groups on raised SBP

Parity	n	%	Raised systolic Blood Pressure (SBP) or medication					
			Unadjusted			Adjusted		
			OR	95% CI		OR		
				Lower	Upper		Lower	Upper
0	42	26.2	0.47	0.22	1.00	0.25	0.06	0.97
1-3	38	34.2	0.69	0.33	1.44	0.72	0.29	1.78
4-6	117	34.2	0.69	0.42	1.13	1.05	0.58	1.88
7-9	165	40.6	0.90	0.58	1.41	1.34	0.81	2.23
10+	153	43.1	1			1		
P-value					0.238			0.126

Adjustment for age, woman's education, husband's education, and marital status

When parity was taken as a continuous variable and SBP kept as a categorical variable as in Table 11-3, an apparent association between parity and SBP was observed in unadjusted analysis. The change in odds of SBP ≥ 140 mmHg or on medication per

extra child (unit change in parity) was 1.06 mmHg (95% CI 1.01 to 1.11, p=0.027). This association was abolished after adjustment for age (data not shown). And when women's educational level, husband's years of schooling and marital status were introduced into the model as confounders in addition to age, the association remained insignificant, as shown in Table 11-3.

Table 11-3: The change of unadjusted and adjusted odds of increased SBP ≥ 140 mmHg per extra child

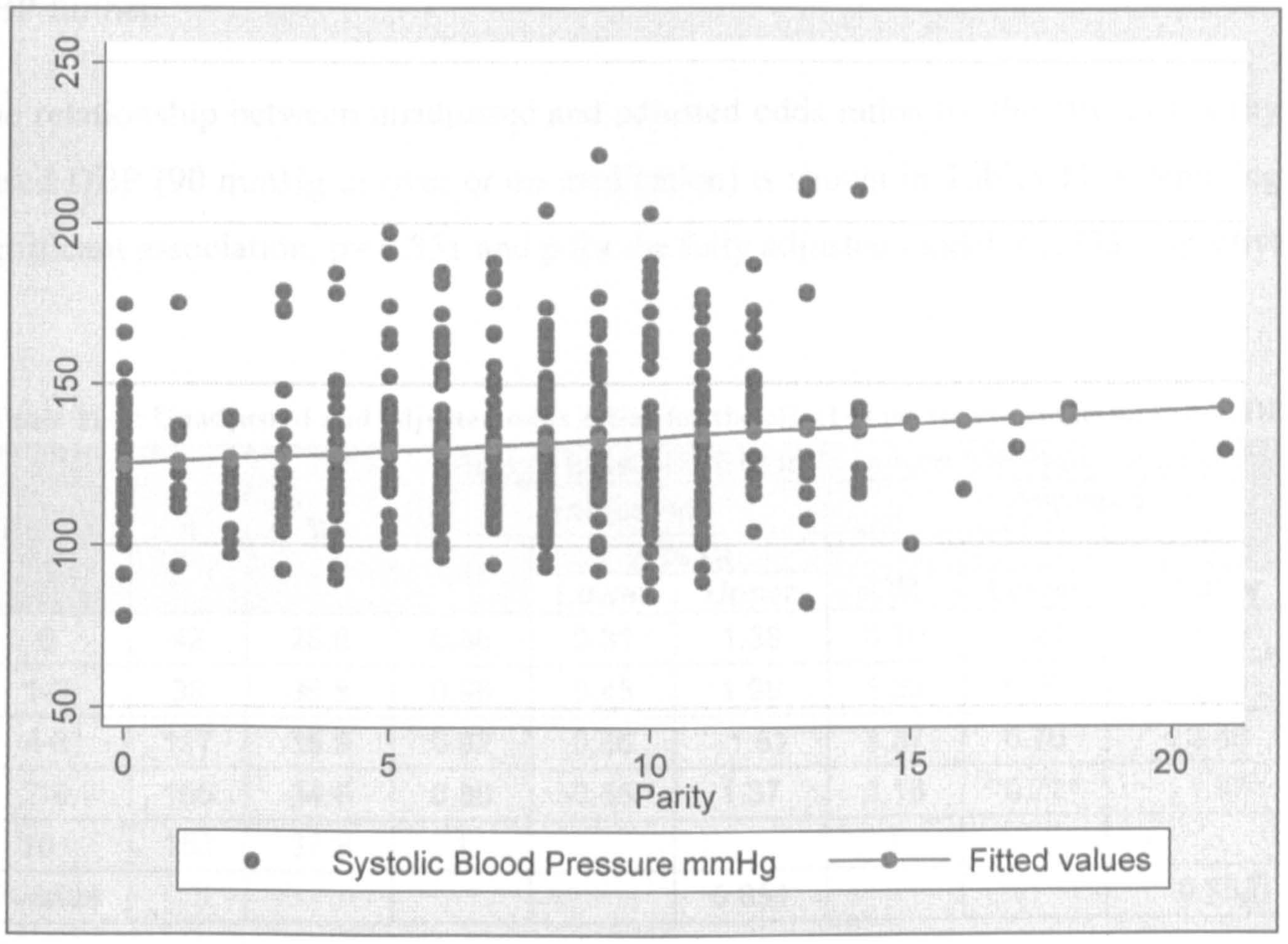
	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.06	0.03	1.01	1.11	0.027
Adjusted for age, educational level, husband's years of schooling and marital status	1.04	0.03	0.97	1.10	0.275

The relationship between systolic blood pressure and parity was also examined with both variables being continuous, using a scatter diagram and by censored ordinary regression. As with FBS, the scatter diagram does not allow for censoring for those on medication, but nevertheless does give a useful picture. An association between parity and SBP was observed in the unadjusted analysis. The regression slope was 0.98, denoting a predicted rise in systolic blood pressure for a unit rise in parity of 0.98 mmHg, (95% CI 0.32 to 1.64, p= 0.004). With adjustment for age, education of both woman and husband and marital status, the magnitude of the association was reduced and its statistical significance disappeared. The significance was lost with adjustment for age alone (not shown in the Table). The difference per increase of one child for age adjusted SBP was 0.34, (95% CI: -0.29 to 0.96, p= 0.289. The scatter diagram with the regression line is shown in Figure 11-1.

Table 11-4: The Unadjusted and Adjusted Regression Slopes of SBP on Parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.98	0.34	0.32	1.64	0.004
Adjusted for age, educational level, husband's years of schooling and marital status	0.31	0.38	-0.43	1.01	0.407

Figure 11-1: Scatter Plot of SBP and Parity



There was no evidence for an association between SBP and parity after adjustment for confounders, and therefore the effect of mediators was not considered in further analysis.

The mean SBP and DBP were compared among those who reported high blood pressure, between those who reported taking medication and those who did not. Women who reported taking the medication had higher DBP and SBP, which might suggest poor adherence. It is for these reasons that women reporting they were on medication were included in the analysis, but with the allowance for censoring to allow for some effect of the medication. It is reasonable to conclude that some women might not comply with taking the medication on regular basis to reduce their DBP and SBP, but nevertheless there would have been some medication effect overall.

11.3 Further Analysis of Parity and Diastolic Blood Pressure (DBP)

In this section, we aim to test the hypothesis that an increasing number of children is associated with an elevation of diastolic blood pressure. As before, initial results were

shown in sections 7-6 and 7-7 and this section takes the relationship between parity and DBP further.

The relationship between unadjusted and adjusted odds ratios for the effect of parity on raised DBP (90 mmHg or over or on medication) is shown in Tables 11-5 depicting no significant association, p= 0.851 and p for the fully adjusted model = 0.753 respectively.

Table 11-5: Unadjusted and adjusted odds ratios for the effect of parity in groups on raised DBP

Parity	n	%	Raised Diastolic Blood Pressure (DBP) or medication					
			Unadjusted			Adjusted		
			OR	95% CI				
				Lower	Upper	OR	Lower	Upper
0	42	28.6	0.66	0.31	1.38	0.70	0.21	2.29
1-3	38	36.8	0.96	0.45	1.99	1.22	0.50	2.99
4-6	117	35.9	0.92	0.56	1.51	1.37	0.76	2.46
7-9	165	34.6	0.86	0.55	1.37	1.18	0.71	1.97
10+	153	37.9	1			1		
P-value					0.851			0.753

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable and DBP was kept as a categorical variable as in Table 11-6, the unadjusted change in odds of DBP ≥ 90 mmHg or on medication per extra child (unit change in parity) was 1.02 (95% CI 0.970 to 1.071, p=0.446), an evidence of no association between parity and DBP in unadjusted analysis. Adjustment did not make a difference to the association and it remained not significant, as in Table 11-6.

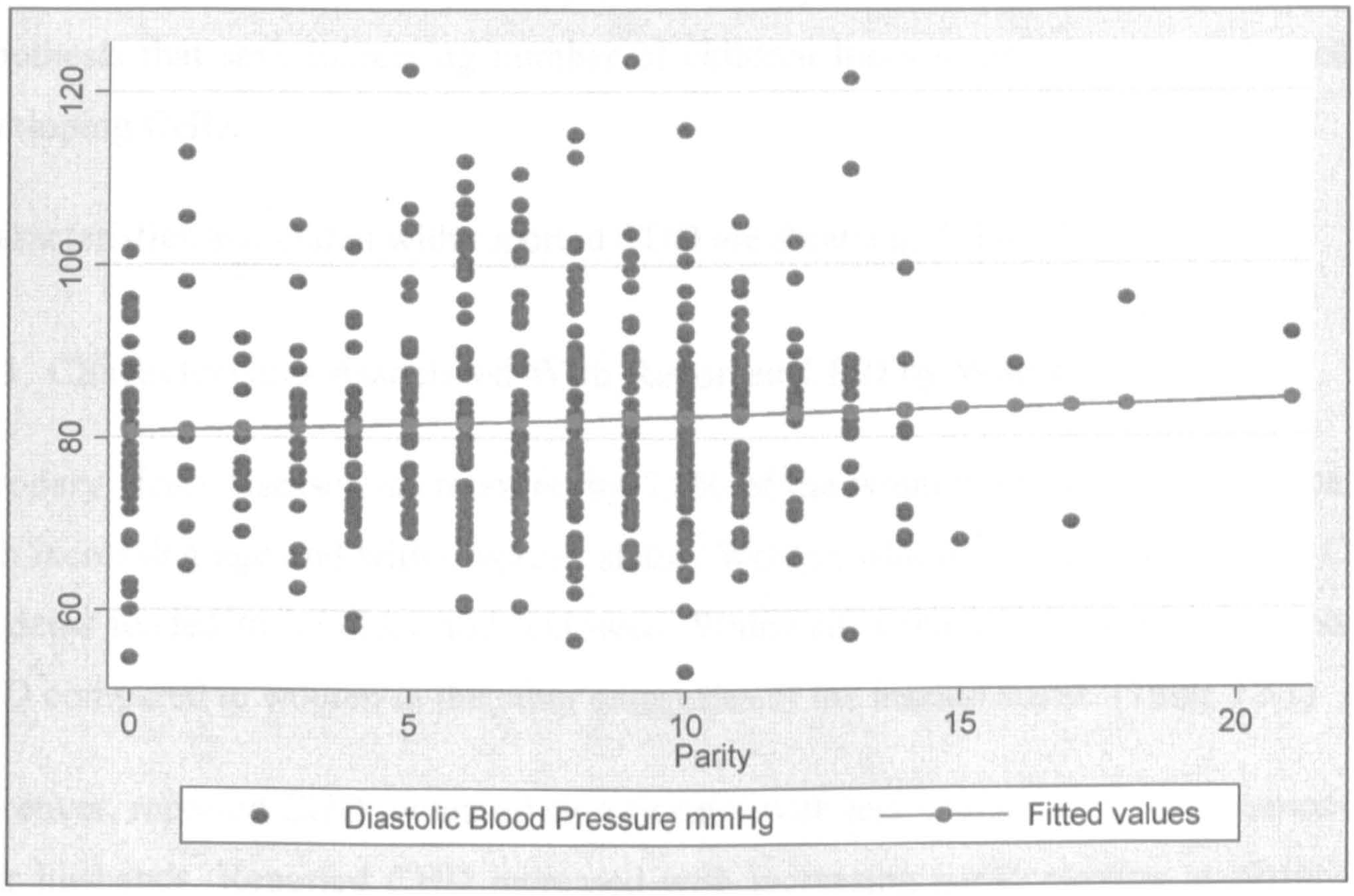
Table 11-6: The change of unadjusted and adjusted odds of increased DBP ≥ 90 mmHg per extra child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.02	0.03	0.970	1.071	0.446
Adjusted for age, educational level, husband's years of schooling and marital status	0.98	0.03	0.92	1.05	0.572

The relationship between diastolic blood pressure and parity was also examined with both variables being continuous, using a scatter diagram and censored ordinary regression. The regression slope was 0.27, giving the predicted rise in diastolic blood

pressure for a unit rise in parity. However, the standard error of this slope coefficient was 0.16 and it was not significant (p=0.094), giving no evidence for an association. The scatter diagram does not allow for censoring for those on medication, but nevertheless does give a useful picture. The scatter diagram of DPB and parity with the regression line is shown in Figure 11-2.

Figure 11-2: Scatter Plot of DBP and Parity



With adjustment for age, women's educational level, husband's years of schooling, and marital status, the slope on the fully adjusted model was reduced and remained insignificant (p=0.916).

Table 11-7: The Unadjusted and Adjusted Regression Slopes of DBP on Parity

	Slope (regression coefficient)	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	0.27	0.16	-0.05	0.59	0.094
Adjusted for age, educational level, husband's years of schooling and marital status	0.02	0.19	-0.35	0.39	0.916

There was no evidence for an association between DBP and parity and therefore effects of mediators were not considered in further analysis.

Chapter 12
REPORTED CORONARY HEART DISEASE (CHD) AND PARITY

So far in the previous sections, we have examined the association between parity and CHD risk factors. In this section we investigated the association between parity and previous coronary heart disease as reported by the women. Section 12.1 discusses the characteristics associated with the reported CHD by women. Section 12.2 discusses the hypothesis that says increasing number of children leads to an increase in the risk of developing CHD.

Characteristics associated with reported CHD are shown in Table 12-1.

12.1 Characteristics Associated With Reported CHD by Women

Coronary Heart disease was reported by 7.8% of the women. It increased significantly with increasing age and with divorced status. Women who reported to have had a CHD incidents tended to be older and widowed. Widowed women had the highest reported CHD compared to women in the other categories of the marital status. (Table 12-1)

Moreover, reported CHD increased significantly with less education of both women and their husbands. Reported CHD increased with increasing parity starting at parity 4-6. Women with parity 0 had the second higher rates of reported CHD at 9.5% followed by parity 1-3. This higher incidence of CHD among the 1-3 parity might be due to the fact that the majority of widows had 1-3 children, and reported CHD was the highest among the widowed. Also reported CHD rates increased with menopausal status. The women, who reported that their periods had stopped, had more CHD than those whose periods had not. Reported CHD by women increased with elevated SBP, DBP and Hypertension. Although these reports of CHD may not be completely reliable, this last finding and the fact that less educated women reported more CHD gives support for some reliability.

Table 12-1: Characteristics Associated with Reported CHD among Women Aged 40-65 Years

Characteristics	Number of women	Women with coronary heart disease (CHD),%	P value
Socio-demographic variables			
Age			**0.009**
<45	159	(3) 1.9	
45-49	115	(11) 9.6	
50.54	110	(9) 8.2	
55-59	95	(12) 12.6	

Characteristics	Number of women	Women with coronary heart disease (CHD),%		P value
60+	35	(5)	14.3	
Women's education, %				**<0.0001**
No formal education	119	(19)	16.0	
Elementary	199	(15)	7.5	
Secondary	167	(6)	3.6	
Higher education	30	(0)	0.0	
Marital status				**0.001**
Married	382	(24)	6.3	
Single	21	(0)	0.0	
Divorced/separated	28	(1)	3.6	
Widowed	84	(15)	17.9	
Currently employed				0.059
No	436	(38)	8.7	
Yes	79	(2)	2.5	
Occupation				0.482
Unskilled worker	16	(0)	0.0	
Skilled worker	14	(1)	7.1	
Employee	24	(0)	0.0	
Private business	25	(1)	4.0	
Husband's education				**0.016**
No formal education	85	(13)	15.3	
Elementary	166	(15)	9.0	
Secondary	170	(10)	5.9	
Higher education	58	(1)	1.7	
Husband currently employed				**0.022**
Yes	241	(14)	5.8	
No	141	(10)	7.1	
Not applicable	112	(16)	14.3	
Own automatic washing machine				0.979
No	400	(31)	7.75	
Yes	115	(9)	7.83	
Family affluence scale				0.966
Poor	225	(18)	8.0	
Average	164	(12)	7.3	
Better off	126	(10)	7.9	
Behavioural risk factors				
Physical activity				0.508
No	445	(36)	8.1	
Yes	69	(4)	5.8	
Smoking status				0.506
Never smoked	481	(38)	7.9	
Ex-smoker	6	(1)	16.7	
Current smoker	28	(1)	3.6	
Watch TV				0.270
No	31	(4)	12.9	

Characteristics	Number of women	Women with coronary heart disease (CHD),%	P value
Yes	484	(36) 7.4	
Hours/week watch TV			0.058
≤ 4	24	(5) 20.8	
5-10	150	(8) 5.3	
11-20	133	(11) 8.3	
21+	177	(12) 6.8	
Stress level			
Human loss and trauma to study subject-1			0.163
No	286	(18) 6.3	
Yes	229	(22) 9.6	
Human loss and trauma to family member-2			0.858
No	328	(26) 7.9	
Yes	187	(14) 7.5	
Property loss to subject-3			0.304
No	510	(39) 7.7	
Yes	5	(1) 20.0	
Work related problems-4			0.412
No	398	(33) 8.3	
Yes	117	(7) 6.0	
All events combined (1-16)			0.287
No	154	(9) 5.8	
Yes	361	(31) 8.6	
Assistance in housework			0.721
No	142	(9) 6.3	
Yes	372	(31) 8.3	
Reproductive health variables			
Parity			**0.038**
0	42	(4) 9.5	
1-3	38	(3) 7.9	
4-6	117	(5) 4.3	
7-9	165	(8) 4.9	
10+	153	(20) 13.1	
Age at 1st marriage, years			0.464
<18	232	(21) 9.1	
18+	262	(19) 7.3	
Age *at 1st birth*			0.303
≤ 18	173	(16) 9.3	
> 18	301	(20) 6.6	
Gravidity 5			0.293
0	38	(2) 5.3	
1- 3	33	(3) 9.1	
4- 6	65	(4) 6.2	
7- 9	136	(6) 4.4	

Characteristics	Number of women	Women with coronary heart disease (CHD),%	P value
10+	243	(25) 10.3	
Age at menarche, years			0.281
≤ 11	39	(3) 7.7	
12	108	(6) 5.6	
13	138	(8) 5.8	
14	133	(16) 12.0	
15+	90	(6) 6.7	
Did you have problems getting pregnant			0.363
No	441	(34) 7.7	
Yes	53	(6) 11.3	
Pregnancy ended as abortion or miscarriage			0.275
No	164	(10) 6.1	
Yes	313	(28) 9.0	
Pregnancy ended as a stillbirth			0.930
No	412	(33) 8.0	
Yes	65	(5) 7.7	
Have you ever had polycystic ovaries			0.548
No	496	(37) 7.5	
Yes	13	(2) 15.4	
Ever use CP			0.463
No	306	(26) 8.5	
Yes	208	(14) 6.7	
Have your periods stopped now			**0.017**
No	285	(15) 5.3	
Yes	229	(25) 10.9	
Age at menopause in years			0.168
≤ 44	44	(2) 4.6	
45-49	75	(11) 14.7	
50-54	95	(12) 12.6	
55+	15	(0) 0.0	
Metabolic risk factors			
Cholesterol (mmol/L)			0.079
Normal	377	(25) 6.6	
Elevated cholesterol	121	(14) 11.6	
LDL-Cholesterol (mmol/L)			0.175
Normal	399	(28) 7.0	
Elevated LDL-chol	99	(11) 11.1	
HDL-Cholesterol (mmo/L)			0.909
Normal	251	(20) 8.0	
Decreased HDL-Chol	247	(19) 7.7	
Triglyceride (mmol/L)			0.502
Normal	343	(25) 7.3	
Elevated TG	155	(14) 9.0	

Characteristics	Number of women	Women with coronary heart disease (CHD),%	P value
T-Cholesterol/LDH-C ratio			0.874
Normal	325	(25) 7.7	
High risk	173	(14) 8.1	
DBP mmHg			**0.007**
Normal	332	(18) 5.4	
Elevated DBP ≥ 90 mmHg/medication	183	(22) 12.0	
SBP mmHg			**0.009**
Normal	318	(17) 5.4	
Elevated SBP ≥ 140 mmHg/medication	197	(23) 11.7	
Hypertension			**0.008**
Normal	295	(15) 5.1	
Hypertensive/medication	220	(25) 11.4	
Diabetic ≥ 1mmol/L or medication			0.414
Normal	400	(29) 7.3	
Elevated FBS	115	(11) 9.6	
Central obesity, WC ≥ 88 cm			0.296
Normal	81	(4) 4.9	
WC ≥ 88 cm	432	(36) 8.3	
BMI			0.808
Non-obese	158	(13) 8.2	
Obese BMI ≥30kg/m^2	355	(27) 7.6	
Abdominal obesity, W/H ratio ≥ 0.85 cm			0.283
Normal	247	(16) 6.5	
WHR ≥ *0.85*	266	(24) 9.0	
Self rating of obesity			0.305
Underweight	21	(4) 19.1	
Normal weight	141	(9) 6.4	
Overweight	228	(16) 7.0	
Obese	94	(8) 8.5	
Very obese	26	(3) 11.5	
Family history of heart diseases			0.642
No	389	(29) 7.5	
Yes	126	(11) 8.7	

12.2 Further Analysis of Parity and Reported CHD

In this section, we aim to test the hypothesis that increasing number of children is associated with an increasing risk of a woman reporting present or past CHD. We have

used the same statistical methods as in the previous chapters for assessing the association between parity and reported CHD.

Tables 12-2 shows the unadjusted and adjusted relationships between reported CHD and parity in groups. The table shows that there was a significant association between parity and reported CHD, P=0.043 in the unadjusted model. Going from parity 10+, the odds ratios decreased, but increased slightly at parity 1-3 and parity 0. The confidence intervals suggested a statistically significant association at parity 7-9 and 4-6, and the percentages reporting CHD were lowest in these groups.

Table 12-2: Unadjusted and adjusted Odds Ratio for the Effect of parity in groups on Reported CHD Events

Parity	n	%	Reported coronary heart disease					
			Unadjusted			Adjusted		
			OR	95% CI				
				Lower	Upper	OR	Lower	Upper
0	42	9.52	0.7	0.23	2.17	1.70	0.42	6.90
1-3	38	7.89	0.57	0.16	2.03	0.64	0.158	2.63
4-6	117	4.27	0.30	0.11	0.82	0.30	0.09	0.99
7-9	165	4.85	0.34	0.145	0.79	0.40	0.16	0.99
10+	153	13.07	1			1		
P-value					0.043			0.082

Adjustment for age, woman's education, husband's education, and marital status

Adjustment for age reduced the association between parity and reported CHD (data not shown in table 12-2) and it was no longer significant. Adjustment for the other confounders as well did not change the non significant effect.

When parity was fitted into the regression model as a continuous variable and reported CHD was kept as a categorical variable as in Table 12-3, the change in the unadjusted odds of CHD events per extra child was 1.05 (95% CI: 0.96-1.15, p=0.249). Adjustment for age, women's education, husband's years of schooling and marital status reduced slightly the magnitude of the association but it remained insignificant.

Table 12-3: The Change of Unadjusted and Adjusted odds of Reported CHD per Extra Child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.05	0.05	0.96	1.15	0.249
Adjusted for age, educational level, husband's years of schooling and marital status	1.01	0.05	0.91	1.11	0.886

Chapter 13
PARITY AND THE METABOLIC SYNDROME

The metabolic syndrome as defined by the International Diabetes Federation (IDF), describes the co-occurrence of abnormalities in glucose and lipid metabolism, central fat distribution and blood pressure.

In the previous sections, we have examined the association between parity and the risk factors for CHD which make up the different components of the metabolic syndrome. In this section we aim to examine if parity plays any role in the development of the metabolic syndrome as such. Section 13.1 sheds lights on the characteristics associated with the metabolic syndrome. Section 13.2 examines the relationship between parity and the combination of these risk factors according to the IDF definition that was described in Appendix 2.

13.1 Characteristics Associated with the Metabolic Syndrome

The metabolic syndrome was presented in 58.3% of the women. In bivariate analysis, women with the metabolic syndrome had significantly higher parity and higher gravidity, p= 0.003 and p= 0.024 respectively. As shown in Table 13-1, women with the metabolic syndrome were significantly older and less likely to have secondary or higher education, were currently unemployed and more likely to be assisted by their daughters or daughters in laws at home, and therefore more likely to be physically inactive. They tended to have elevated DBP, SBP and hypertension and were more frequently menopausal. They tended to have higher rates of obesity, central and abdominal obesity compared to those women without the metabolic syndrome. The metabolic syndrome was more prevalent among married and widowed women. Differences between those with and without the metabolic syndrome, with respect to several socio-demographic, reproductive and behavioural risk factors are shown in Table 13-1.

Table 13-1: Characteristics Associated with the Metabolic Syndrome among Women

Characteristics	Number of women	Women with metabolic syndrome %	Women without metabolic syndrome, %	P- value*
Socio-demographic variables				
Age				**<0.0001**
<45	154	(58) 37.7	(96) 62.3	
45-49	111	(66) 59.5	(45) 40.5	
50.54	105	(72) 68.6	(33) 31.4	
55-59	91	(67) 73.6	(24) 26.4	
60+	34	(26) 76.5	(8) 23.5	
Women's education, %				**<0.0001**
No formal education	113	(79) 69.9	(34) 30.1	
Elementary	194	(126) 65.0	(68) 35.0	
Secondary	161	(78) 48.5	(83) 51.5	
Higher education	28	(6) 21.4	(22) 78.6	
Marital status				**0.045**
Married	371	(212) 57.1	(159) 42.9	
Single	21	(11) 52.4	(10) 47.6	
Divorced/separated	26	(11) 42.3	(15) 57.7	
widowed	78	(55) 70.5	(23) 29.5	
Currently employed				**0.014**
No	421	(255) 60.6	(166) 39.4	
Yes	75	(34) 45.3	(41) 54.7	
Occupation				0.425
Unskilled worker	15	(9) 60.0	(6) 40.0	
Skilled worker	13	(5) 38.5	(8) 61.5	
Employee	23	(8) 34.8	(15) 65.2	
Private business	24	(12) 50.0	(12) 50.0	
Husband's education				0.088
No formal education	80	(52) 65.0	(28) 35.0	
Elementary	160	(100) 62.5	(60) 37.5	
Secondary	167	(92) 55.1	(75) 44.9	
Higher education	54	(25) 46.3	(29) 53.7	
Husband currently employed				0.445
Yes	237	(133) 56.1	(104) 43.9	
No	134	(79) 59.0	(55) 41.0	
Not applicable	104	(66) 63.5	(38) 36.5	
Own automatic washing machine				0.152
No	387	(232) 60.0	(155) 40.0	
Yes	109	(57) 52.3	(52) 47.7	
Family affluence scale				0.880
Poor	218	(128) 58.7	(90) 41.3	
Average	157	(89) 56.7	(68) 43.3	
Better off	121	(72) 59.5	(49) 40.5	

Characteristics	Number of women	Women with metabolic syndrome %	Women without metabolic syndrome, %	P- value*
Behavioural risk factors				
Physical activity				**<0.0001**
No	429	(266) 62.0	(163) 38.0	
Yes	66	(23) 34.9	(43) 65.1	
Smoking status				0.909
Never smoked	463	(269) 58.1	(194) 41.9	
Ex-smoker	6	(4) 66.7	(2) 33.3	
Current smoker	27	(16) 59.3	(11) 40.7	
Watch TV				0.728
No	29	(16) 55.2	(13) 44.8	
Yes	467	(273) 58.5	(194) 41.5	
Hours/week watch TV				0.445
≤ 4	23	(16) 69.6	(7) 30.4	
5-10	144	(78) 54.2	(66) 45.8	
11-20	129	(79) 61.2	(50) 38.8	
21+	171	(100) 58.5	(71) 41.5	
Stress level				0.096
All events combined				
No	142	(91) 64.1	(51) 35.9	
Yes	354	(198) 55.9	(156) 44.1	
Assistance in housework				**0.019**
No	131	(65) 49.6	(66) 50.4	
Yes	365	(224) 61.4	(141) 38.6	
Reproductive health variables				
Parity				**0.003**
0	40	(21) 52.5	(19) 47.5	
1-3	33	(11) 33.3	(22) 66.7	
4-6	110	(62) 56.4	(48) 43.6	
7-9	160	(90) 56.3	(70) 43.7	
10+	153	(105) 68.6	(48) 31.4	
Age at 1st marriage, years				0.129
<18	227	(141) 62.1	(86) 37.9	
18+	248	(137) 55.2	(111) 44.8	
Age at 1st birth				0.095
≤ 18	168	(107) 63.7	(61) 36.3	
> 18	289	(161) 55.7	(128) 44.3	
Gravidity 5				**0.024**
0	36	(20) 55.6	(16) 44.4	
1- 3	29	(10) 34.5	(19) 65.5	
4- 6	60	(30) 50.0	(30) 50.0	
7- 9	130	(76) 58.5	(54) 41.5	
10+	241	(153) 63.5	(88) 36.5	

Characteristics	Number of women	Women with metabolic syndrome %		Women without metabolic syndrome, %		P- value*
Age at menarche, years						0.127
≤ 11	37	(19)	51.4	(18)	48.6	
12	103	(69)	67.0	(34)	33.0	
13	132	(81)	61.4	(51)	38.6	
14	131	(72)	55.0	(59)	45.0	
15+	87	(44)	50.6	(43)	49.4	
Did you have problems getting pregnant						0.110
No	425	(254)	59.8	(171)	40.2	
Yes	50	(24)	48.0	(26)	52.0	
Pregnancy ended as abortion or miscarriage						0.149
No	156	(84)	53.9	(72)	46.1	
Yes	304	(185)	60.9	(119)	39.1	
Pregnancy ended as a stillbirth						0.156
No	397	(227)	57.2	(170)	42.8	
Yes	63	(42)	66.7	(21)	33.3	
Have you ever had polycystic ovaries						0.359
No	476	(276)	58.0	(200)	42.0	
Yes	13	(9)	69.2	(4)	30.8	
Ever use CP						0.868
No	291	(169)	58.1	(122)	41.9	
Yes	204	(120)	58.8	(84)	41.2	
Have your periods stopped now						**<0.0001**
No	277	(138)	49.8	(139)	50.2	
Yes	218	(150)	68.8	(68)	31.2	
Age at menopause in years						0.056
≤ 44	42	(23)	54.8	(19)	45.2	
45-49	72	(47)	65.3	(25)	34.7	
50-54	89	(69)	77.5	(20)	22.5	
55+	15	(11)	73.3	(4)	26.7	
Metabolic risk factors						
Cholesterol (mmol/L)						**0.001**
Normal	376	(204)	54.3	(172)	45.7	
Elevated cholesterol	120	(85)	70.8	(35)	29.2	
LDL-Cholesterol (mmol/L)						**<0.0001**
Normal	398	(214)	53.8	(184)	46.2	
Elevated LDL-chol	98	(75)	76.5	(23)	23.5	
HDL-Cholesterol (mmol/L)						**<0.0001**
Normal	250	(110)	44.0	(140)	56.0	
Decreased HDL-Chol	246	(179)	72.8	(67)	27.2	

Characteristics	Number of women	Women with metabolic syndrome %		Women without metabolic syndrome, %		P- value*
Triglyceride (mmol/L						**<0.0001**
Normal	341	(137)	40.2	(204)	59.8	
Elevated TG	155	(152)	98.1	(3)	1.9	
T-Cholesterol/LDH-C ratio						**<0.0001**
Normal	324	(156)	48.2	(168)	51.8	
High risk	172	(133)	77.3	(39)	22.7	
DBP mmHg						**<0.0001**
Normal	321	(145)	45.2	(176)	54.8	
Elevated DBP ≥ *90 mmHg/or on medication*	175	(144)	82.3	(31)	17.7	
SBP mmHg						**<0.0001**
Normal	308	(133)	43.2	(175)	56.8	
Elevated SBP ≥ *140 mmHg or on medication*	188	(156)	83.0	(32)	17.0	
Hypertension						**<0.0001**
Normal	285	(112)	39.3	(173)	60.7	
Hypertensive	212	(177)	83.9	(34)	16.1	
Diabetic ≥7.00 mmol/L or on medication						**<0.0001**
Normal	399	(198)	49.6	(201)	50.4	
Elevated FBS	97	(91)	93.8	(6)	6.2	
Anthropometric Factors						
Central obesity, WC ≥ 88 cm						**<0.0001**
Normal	79	(16)	20.3	(63)	79.7	
WC ≥ *88 cm*	417	(273)	65.5	(144)	34.5	
BMI						**<0.0001**
Non-obese	153	(64)	41.8	(89)	58.2	
Obese BMI ≥30kg/m^2	343	(225)	65.6	(118)	34.4	
Abdominal obesity, W/H ratio ≥ 0.85 cm						**<0.0001**
Normal	242	(112)	46.3	(130)	53.7	
WHR ≥ *0.85*	254	(177)	69.7	(77)	30.3	
Self rating of obesity						**0.010**
Underweight	20	(6)	30.0	(14)	70.0	
Normal weight	137	(72)	52.6	(65)	47.4	
Overweight	217	(128)	59.0	(89)	41.0	
Obese	93	(61)	65.6	(32)	34.4	
Very obese	24	(18)	75.0	(6)	25.0	
Components of the metabolic syndrome as defined by IDF						
Fasting glucose ≥ 5.6 mmol/L (100 mg/dl)						**<0.0001**
Normal	354	(152)	42.9	(202)	57.1	
Elevated FBS	142	(137)	96.5	(5)	3.5	

Characteristics	Number of women	Women with metabolic syndrome %		Women without metabolic syndrome, %		P- value*
DBP ≥ 85 mmHg						**<0.0001**
Normal	317	(135)	42.6	(182)	57.4	
Elevated DBP ≥ *85 mmHg*	179	(154)	86.0	(25)	14.0	
SBP ≥ 130 mmHg						**<0.0001**
Normal	273	(96)	35.2	(177)	64.8	
Elevated SBP ≥ *130 mmHg*	223	(193)	86.6	(30)	13.4	
Hypertension ≥ 130/85 mmHg						**<0.0001**
Normal	248	(76)	30.7	(172)	69.3	
Hypertensive	248	(213)	85.9	(35)	14.1	
Fasting HDL-C < 1.3 mmol/L (50 mg/dl)						**<0.0001**
Normal	110	(21)	19.1	(89)	80.9	
Decreased HDL-Chol	386	(268)	69.4	(118)	30.6	
Fasting Triglyceride ≥ 1.7 mmol/L (150 mg/dl)						**<0.0001**
Normal	341	(137)	40.2	(204)	59.8	
Elevated TG	155	(152)	98.1	(3)	1.9	
Waist circumference ≥ 80 cm						**<0.0001**
Normal	31	(0)	0.0	(31)	100.0	
WC ≥ *80 cm*	465	(289)	62.2	(176)	37.8	

[1] P value compare those with the metabolic syndrome to those without the metabolic syndrome, are results of χ^2 statistics for categorical variables.

13.2 Further Analysis of Parity and the Metabolic Syndrome

In this final section, we aim to test the hypothesis that an increasing number of children is associated with an increasing prevalence of the metabolic syndrome. The same statistical methods as in the previous chapter of parity and reported CHD were used in assessing the association between parity and the prevalence of the metabolic syndrome.

A significant association between parity in groups and the prevalence of the metabolic syndrome was observed, p=0.024 as shown in Table 13-2. The prevalence of the metabolic syndrome decreases with less parity and rises again at parity 0. Adjustment for age increased slightly the magnitude of the association and the association remained significant, p=0.038. Adjustment for educational level attenuated the

association to the null hypothesis more and it became non significant, p= 0.141, (results not shown). Further adjustments for husband's educational level and marital status did not make a difference to the magnitude of the association and it remained non significant as shown in Table 13-2.

Table 13-2: Unadjusted and adjusted Odds Ratio for the Effect of Parity in groups on the Prevalence of the Metabolic Syndrome

Parity	n	%	Prevalence of metabolic syndrome (MS)					
			Unadjusted			Adjusted		
			OR	95% CI		OR		
				Lower	Upper		Lower	Upper
0	40	52.5	0.51	0.25	1.02	0.56	0.18	1.70
1-3	33	33.3	0.23	0.10	0.51	0.28	0.11	0.72
4-6	110	56.4	0.59	0.36	0.98	0.90	0.50	1.62
7-9	160	56.3	0.59	0.37	0.93	0.70	0.42	1.15
10+	153	68.6	1			1		
P-value					0.024			0.076

Adjustment for age, woman's education, husband's education, and marital status

When parity was fitted into the regression model as a continuous variable with the prevalence of the metabolic syndrome kept as a binary variable as in Table 13-3, the change in the unadjusted odds of the metabolic syndrome per extra child was 1.09 (95% CI: 1.04 to 1.15, p=0.001). Adjustment for age reduced the magnitude of the association, but it remained significant, p= 0.028. A 7% increase in the prevalence of the metabolic syndrome per extra child was observed when the association was adjusted for age, women and husband's education and marital status, p= 0.042.

Table 13-3: The Change of Unadjusted and Adjusted Odds of the Prevalence of Metabolic Syndrome per Extra Child

	Odds ratio	SE	95% CI		Statistical significance
			Lower	Upper	
Unadjusted	1.09	0.03	1.04	1.15	0.001
Adjusted for age, educational level, husband's years of schooling and marital status	1.07	0.04	1.00	1.14	0.042

13.3 Other Characteristics and Mediators

The analysis is taken further, and details of the role of mediators and other correlates are shown in Table 13-4. In these regression models, all variables that were

significantly associated with the prevalence of the metabolic syndrome were introduced into the model separately to test their roles individually and to test if they act as mediators in the relationship between parity and the metabolic syndrome. Only those that still showed a significant association with metabolic syndrome were kept in the model.

None of the changes in the odds ratio for parity were very marked. With physical activity and abdominal obesity it changed only from 1.07 to 1.06. For overall obesity (BMI $\geq$ 30 kg/m^2), the change was from 1.07 to 1.05, suggesting a possible small mediation from this source. It is interestingly noticeable that BMI is highly correlated with WC, a component of the definition of the metabolic syndrome, and therefore its role here is very trivial.

Table 13-4: Effect of Mediators along the Causal Pathway Between Parity and the Metabolic Syndrome after Adjusting for Confounders Age, Women and Husband's Education and Marital Status

Additional characteristics (mediators)	Change in odds of positive MS per extra child	95% CI		P value	Change in odds of positive MS for change in the mediator	95% CI		P Value
		lower	upper			Lower	Upper	
Unadjusted	1.09	1.04	1.15	0.001				
Fully adjusted	1.07	1.00	1.14	0.042				
Physical activity	1.06	0.995	1.14	0.066	0.37	0.20	0.69	0.002
Obese	1.05	0.979	1.12	0.175	2.23	1.42	3.51	0.001
Abdominal obesity	1.06	0.997	1.14	0.063	2.03	1.35	3.07	0.001

Chapter 14
DISCUSSION

This discussion summarizes the main findings; it then addresses the uniqueness of the study and then some methodological considerations, including the strengths and limitations of the approaches used. This is followed by an interpretation of the results regarding the association between parity and each CHD risk factors, reported CHD and the metabolic syndrome. Finally the implications of the results of the study for public health and research are presented.

14.1 Summary of Main Findings within the context of Arab Women

A total of 515 women from two refugee camps, Amaari and Kalandia, participated in the study. The majority of the women in the study were married at a younger age than the national average of 19.4 years. Approximately 59% of women who were ever married had married young, below or at the age of 18 years (the minimum age at first marriage was 11.5 and maximum age was 41 years). Of these 23.7% married early, below 16 years of age. They were also married at a younger age than neighbouring Arab countries, where early marriage is seeing a downward trend—most notably in Kuwait, Libya, and the United Arab Emirates. For the region as a whole, women are marrying later (some in their late 20s or early 30s), and some women are not marrying at all. In Tunisia, Algeria, and Lebanon, only 1%-4% of women ages 15 to 19 are married, and the percentage of women ages 35 to 39 who have never married in these countries now ranges from 15 percent to 21 percent [281]. This is dramatically lower than the women surveyed, where over 40% were married by the age of 18, and only 4% were not married at all.

The majority were married and living with their husbands, and the average family size was 7.4. Compared to Arab women, Palestinian women share high fertility rates and correspondingly high birth rates; this is a direct effect of early marriage. This relatively high rate of early marriage is due largely to custom and to the economic and social constraints which oblige parents to marrying their daughters in order to lessen household expenditures. Early marriage has a direct correlation to higher birth rates. In the study, the number of children per woman ranged from 0 to 21. The women surveyed were found to have born on average 7.3 live children in their lifetime

(median 8). This is also significantly higher than the national average. The crude birth rate in 2006 was 36.7 (41.7 in Gaza Strip and 33.7 in West Bank) per 1000 population [18]. The fertility rate in 2006 was also high at 4.6 births per woman (5.4 in the Gaza Strip and 4.2 in the West Bank) [17] [19].

Birth rates differ greatly from one Arab country to the next. The fertility rate in the Arab world, ie 3.5 births per woman, is higher than the world's average of 2.7 [282]. Some Arab countries, notably Tunisia, the United Arab Emirates, Bahrain, Kuwait and Lebanon, are either below or very close to that stability level of 2.1. Algeria and Morocco, at 2.4, are dropping fast toward it [283]. This is significantly lower than Palestine's average of 4.6.

Marriage was not the only area where the Palestinian women in the study differed from the national average or those of their Arab neighbours. The refugee women's participation in the labour force was low and the vast majority (84.7%) were unemployed. Out of the 79 study women employed, 20.3% were unskilled workers and 31.6% worked in small private businesses. Compared to the national average of 14.1%, employed women in the study are faring slightly better with a percentage 15.3% of the women in employment. However, Palestinian women's participation in the labour force was much lower than their Arab neighbours. In Lebanon, 29% of women are employed, and almost 25% of them worked in the professional sector. Morocco has an even higher rate of working women, where 35% of women are employed. One-third of doctors and one-quarter of university professors in Morocco are women. In Syria and Algeria, 28% and 36% of women are employed respectively [284].

Although Palestinian women lagged behind the region in women in the labour force, they are faring better in the realm of education. Approximately 75% of the women in the refugee camp had some formal education, 23% had none, and the former only had a mean of 5.62 years of education. This is somewhat lower than the national average where 88% of Palestinian women are literate, indicating a higher rate of education [285]; however, it remains higher than the regional average for literacy rates.

For the majority of Arab countries, the proportion of illiterate women constitutes between a third and two-thirds of adult women with a significant difference between

women and men. Female literacy rates for girls 15 and over in the Arab world ranges from 24% (Iraq) to 85.9 percent (Jordan). The most recent data reveals that such literacy rates range from 80% and above in ten countries (Jordan, United Arab Emirates, Bahrain, Saudi Arabia, Syria, Kuwait, Lebanon, Qatar, Palestine and Libya), which are relatively small states with the exception of Saudi Arabia, to less than 75% in nine other countries with large populations, with Iraq and Yemen standing as low as 40% and 49% respectively [286].

While literacy rates are improving, noncommunicable diseases are increasing across the board in the Arab World. In Jordan, for example, the leading cause of reported deaths for males (37.9%) and females (38.6%) are those related to diseases of the cardiovascular system [287].

According to the World Health Organization strategy *At a Glance*, amongst Palestinian refugees, noncommunicable diseases are the major causes of mortality (heart disease 19.1%, cerebrovascular conditions 8.2%, cancers 9.9%, and a sharp increase in accidents from 9 per 100 000 in 1995 to 32.2 per 100 000 in 2004 [288].

Weight, BMI, and waist circumference, are among the risk factors for cardiovascular disease under study for their associations with parity. In our study, the average weight of the women was 80.6 kg and height was 1.56 metres, resulting in a mean BMI of 33.3 kg/m^2. Using BMI$\geq$ 30 kg/m^2 to indicate overall obesity, the majority of the women (69.2%) were obese. The women's mean waist circumference was 98.0 cm, mean hip circumference was 115.5 cm, and mean waist to hip ratio was 0.85 cm. The prevalence of central obesity (WC $\geq$ 88 cm) was 84.2% and the prevalence of abdominal obesity (W/H ratio $\geq$ 0.85 cm) was 51.9%. The majority of women were obese whether in terms of overall obesity or abdominal adiposity.

The prevalence of hypertension and diabetes including those on medication was 42.7% and 22.3%, respectively. The women's lipid profile was as follows: 24.3% had elevated total cholesterol, 31.1% had elevated triglycerides, and 49.6% had HDL-C levels below 1 mmol/L (40 mg/dl). The women had mean fasting plasma insulin of 9.5 uIU/ml.

The metabolic syndrome was found in 58.3% of the women and 7.8% reported having had a CHD event. Using the Framingham risk score and excluding those women who already have a CHD event from the analysis, 5.7% of women were found to be at high risk for the development of CHD in 10 years, and 16.9% at medium risk of developing CHD in 10 years.

The analysis indicates a significant association of BMI, WC with parity, independent of socioeconomic, behavioural and other reproductive risk factors. The adjusted regression coefficient of BMI on parity is 0.30 (95% CI: 0.14 to 0.47, p<0.001); and the adjusted regression coefficient of WC is 0.58 (95% CI: 0.25 to 0.91, p= 0.001). Other covariates that may have acted as mediators did not explain these associations, except for assistance in housework (where it partially accounted for some effect, but the association still remained significant. The adjusted regression coefficient of assistance in household on BMI and WC is 0.23 (95% CI: 0.060 to 0.40, p=0.008) and 0.43 (95% CI: 0.09 to 0.76, p=0.013) respectively. The study did not provide evidence of an association between W/H ratio and parity. The adjusted regression coefficient of W/H ratio on parity is 0.0010 (95% CI: -0.0009 to 0.0028, p=0.308).

The results also show that among the lipid and lipoproteins levels, only triglycerides were significantly associated with parity (adjusted regression coefficient is 0.036 (95% CI= 0.003 to 0.068, p=0.033), and the association appears to be mediated partially by BMI (adjusted regression coefficient is 0.027 (95% CI: -0.006 to 0.060, p= 0.111) and WC (adjusted regression coefficient is 0.025 (95% CI: -0.008 to 0.057, p=0.137) and sedentary life style (adjusted regression coefficient is 0.025 (95% CI: -0.009 to 0.058, p= 0.147); and finally by being diabetic (adjusted regression coefficient is 0.028 (95% CI: -0.003 to 0.059, p= 0.078).

An unadjusted association between the T-CHOL/HDL-C ratio and parity was observed. However, this was attenuated after adjustment for age, and was completely removed (regression coefficient 0.008 [95% CI: 0.0006 to 0.002, p=0.282]) after adjustment for women's educational level, husband's years of schooling and marital status, as in Table 9-17.

No significant association was observed between parity and type 2 diabetes mellitus after adjustment for age. However, a statistically significant association between

gravidity and type 2 diabetes was observed in unadjusted and adjusted analyses (adjusted regression coefficient is 0.14 (95% CI: 0.05 to 0.23, p=0.002). There was also an association with presumed pregnancy losses, calculated by subtracting parity from gravidity; this suggests a role of failed pregnancies in the risk of diabetes, although these results should be regarded with caution because an association of diabetes and gravidity, but not parity, was not expected nor supported elsewhere and many statistical tests were performed.

Our results showed an association between parity and SBP in an unadjusted analysis. Adjustment for age and other confounders (women's education, husband's education and marital status) attenuated the association. Regression coefficient is 0.31 (95% CI: -0.43 to 1.01, p=0.407). Our results showed no evidence of an association between parity and DBP. Regression coefficient is 0.02 (95% CI: -0.35 to 0.39, p=0.916).

Analyses were also aimed to determine if parity increases the risk of CHD and the development of the metabolic syndrome among these women. A total of 7.8% of women reported having had a CHD event. A marginally significant association was observed between parity and reported CHD events (p=0.043). Adjustment for age attenuated this association, which was no longer significant, p= 0.192. When parity was fitted in a logistic regression model as a continuous variable and reported CHD was kept as a categorical variable, the change in the unadjusted odds of CHD events per extra child was 1.05 (95% CI: 0.96-1.15, p=0.249). No significant association was observed between parity and reported CHD among these women.

The metabolic syndrome presented in 58.3% of the women. Women with the metabolic syndrome had significantly higher parity and higher gravidity, p= 0.003 and p= 0.024 respectively. A 7% increase in the prevalence of the metabolic syndrome per extra child was observed in logistic regression with adjustment for age, women's and husband's education and marital status, (p= 0.042).

Further analysis suggested that physical inactivity, overall obesity and abdominal obesity factors slightly mediate the association between parity and the metabolic syndrome, Adjusted regression coefficients are as follows and respectively: 1.06 (95% CI: 0.995 to 1.14, p=0.066); 1.05 (95% CI: 0.979 to 1.12, p=0.175); 1.06 (95% CI: 0.977 to 1.14, p=0.063).

In a separate analysis excluding all women with reported CHD events, 5.7% of women were considered to be high CHD risk for the next 10 years and 16.9% were considered to be moderate CHD risk for the next 10 years.

14.1.1 Support for the Hypotheses

The relationship between the outcome variables of interest and parity, as summarized above, were assessed using different statistical models. All results were found to be consistent between crude and multivariate results. Most associations that were significant in univariate analysis were attenuated by adjustment although some continued to remain significant. However, not all hypotheses were supported. In so far as it is reasonable to expect positive relationships similar to the evidence in other studies, the non-significant findings could be due to lack of statistical power and the small sample size especially for the lowest levels of parity.

14.1.2 Uniqueness of the Study

This study is unique in many ways. First, it is the first time five different risk factors (overall obesity, central and abdominal adiposity, hyperlipidemia, diabetes and hypertension) for heart disease were studied. Second, this study focused on the association between CHD risk factors and parity among women, aged 40-65 years old, who have completed their child bearing. The women in this study are from a population with one of the highest fertility rates in the world, (with an average of 7.3 children and a median of 8 children (range of 0-21 children), who therefore may have a higher risk for diseases that are associated with parity. And there is a significant lack of data on the health status of refugee women in particular.

It is relevant to note that this group of Palestinian refugee women was homogeneous in terms of their religious beliefs (all were Moslem), educational level and general socioeconomic status. They shared other special features that may distinguish them from western populations, namely a low prevalence of smoking, no alcohol use, physical inactivity and frequent child births. One consequence of this, also a special feature of this study, is that confounding is likely to pay less of a strong effect. Of course, adjustment for confounders was still applied, although residual and unidentified confounding may well have played a smaller role.

The population under study also has other unusual features. It is extremely rare for a woman to remain single in the Palestinian society, especially in a refugee camp environment. Usually Palestinian women do not remain single out of choice, but due to an inability to marry. Likewise, it can be assumed that nulliparity is also not by choice. A couple that remains childless is most probably experiencing infertility. In this study, 42 women out of the 515 women were nulliparae; 21 nulliparae were single (not married) and the other 21 nulliparae were married and had either a quick onset of separation or widowhood or couple infertility was involved. The nulliparae are therefore rather different, both socially and possibly biologically, from the rest of the married women. This calls into question comparisons of this group with other societies. However, analysis is constrained by the small size of the group of nulliparae, so comparisons in the data analysis lack statistical power. However, comparisons with other studies were possible when looking at the difference in mean outcome variable per extra child and at the percentage of change (increase or decrease) in outcome variable per extra child.

14.1.3 Methodological Limitations

Various methodological limitations of the analysis and ways of addressing them are detailed below under each CHD risk factor and parity. As a cross-sectional study, the results of this study are susceptible to several sources of bias, such as recall bias, selection bias, participation bias, and survival bias. As the analyses are all cross sectional, it is not strictly possible to attribute causality in the associations found. Nevertheless observed associations between parity and CHD risk factors are unlikely to be due to reverse causality. Residual confounding due to unmeasured or unanalyzed variables related to both the exposure and the outcome variables, and thus responsible for the association, could not be ruled out.

A further limitation arises because a large number of associations were tested statistically, so it is likely that more of them that were found significant were actually due to chance than the formal significance level implies, leading to an uncertainty in interpreting how much evidence for an association is given by the results of the tests of the association. Therefore the levels of significance are not the only source of evidence for the different associations, but also other evidence is also considered

alongside the results in this study. The other evidence comes when the findings agree with reports from other studies, and where scientifically valid mechanisms can support the association.

These methodological limitations and others will be discussed in more detail in the following sections relating parity to CHD risk factors.

14.1.4 Considerations for Causality

Nine criteria for causality proposed by Hill [289] are considered here. Our study satisfies some of them but not all. The first criteria to show causality are:

1. Temporal Relationships:

Since our study is a cross sectional study, the timing of events were not directly observed. Some events such as age at first marriage and age at first pregnancy were reported as occurring earlier than some of the outcomes. The most obvious is that parity and childbearing occurred before the various observed levels of risk factors. So childbearing preceded their current HDL-C, Cholesterol, Triglycerides, and waist circumference, BMI, Diabetes and Hypertension. For Hypertension and Diabetes we have age at onset for both outcomes, so in order to make sure that Hypertension and Diabetes was not present before the last pregnancies when looking at the relationship between parity and diabetes on one hand and between parity and Hypertension on the other, we excluded all the women who had diabetes and hypertension before they were pregnant; this was so for one case for diabetes and 2 cases of hypertension which were excluded in order to make sure that pregnancies came before diabetes when we look at the association of pregnancy and diabetes. For the other outcomes variables such as the lipids, we don't have the date of onset, and therefore we might not be able to satisfy this criterion. But we assume that such diseases take place at older age and would make more sense that these women had children before developing hyperlipidemia. Interpreting the associations found between parity and BMI and WC in terms of causality is difficult in a cross-sectional study, but the high and independent associations observed in this study speak in favour of a causal relation. There might be biological mechanisms that could in part explain a causal relationship. For example, certain sex hormones or other internal or external

factors might both determine the distribution of adipose tissue and the degree of adiposity. There are also likely to be behavioural pathways, as are shown by the mediation by help with housework

2. Strength:

The strength of the association between an exposure and an outcome variable is measured by the magnitude of the association such as odds ratio or regression coefficient. The stronger the magnitude of the association the more likely that the relation is causal. In our study, the magnitude for associations between parity and each of the outcome variables was modest, so these associations are not supported on these grounds in terms of cause and effect. The only outcomes that show somehow stronger magnitudes are BMI and WC with parity. Adjusted regression coefficient of BMI is 0.30 (95% CI: 0.14 to 0.47, $p<0.001$); and adjusted regression coefficient of WC is 0.58 (95% CI: 0.25 to 0.91, $p= 0.001$). After taking into consideration mediating effect, the association remained significant. Adjusted regression coefficient of assistance in household on BMI and WC is 0.23 (95% CI: 0.060 to 0.40, $p=0.008$) and 0.43 (95% CI: 0.09 to 0.76, $p=0.013$) respectively.

3. Dose Response relationship:

In our study, increasing number of children is associated with the increasing risk of developing CHD risk factors. The scatter diagram for example, confirms the linear relationship between parity and obesity where one can see some kind of a uniform rise and the regression coefficient demonstrated a linear association of BMI and parity where one can reasonably accept an increase in BMI per additional child. The trends in odds ratios and mean differences with parity in ascending groups also suggest a dose response. The same applies to WC.

4. Consistency:

The association between parity and CHD risk factors has been studied in different settings and among different populations including the Palestinian setting. This study presents similarity of results to those studies in other settings. All results show that parity (increasing number of children) increases the risk of developing

raised CHD risk factors. For example, the results of this study were consistent with previous studies that examined the association between parity and BMI among women who have completed their childbearing years. Weng et al [126] found a 7% increase in risk of obesity for each additional child after adjusting for confounders, while Bastian et al [154], found an 11% increase in risk of obesity with each additional child that was independent of socioeconomic status and other confounders. Both studies used data from the Utah population where the majority was Mormon and women bore many children. In this study, there was a 14% increase (95% CI: 1.07 to 1.22, p <0.0001) in risk of obesity with each additional child after adjusting for confounders. The same applies for other risk factors such as Triglycerides where it increases with increasing parity, where as higher parity is unlikely to have an important impact on the development of type II in this study similar to results from the US and other industrialized countries.

5. Plausibility:

In this study, an independent association was found between parity and BMI, on one hand, and parity and WC, on the other. These independent associations are not explained by potential confounders and mediators, and are supported in other studies, and are more likely to represent a biological response to pregnancy. Bahavioural factors are also likely to apply. Changes in lifestyle accompanying raising children such as assistance in housework partially mediated the association, but because the association remained significant it seems to have an influence beyond these mediators. It is always possible that the association is due to unmeasured or residual confounders that we could not control for in our analysis.

Triglycerides (TG) showed a significant association with parity that was not explained by confounders. Increased TG levels in women with more children appeared to be partially mediated by BMI and assistance in housework. This suggests that the relationship between parity and triglycerides levels could be associated with the long term biological consequences of pregnancy through the alterations of lipid levels. The weight increase associated with pregnancy and/or the sedentary life style the women are leading partially took some of the effect of parity, but the association remained significant.

Also in this study, a 7% increase in the prevalence of the metabolic syndrome per extra child was observed when the association with ungrouped parity was adjusted for age, women's and husband's education and marital status, p= 0.042. The association between parity and metabolic syndrome appears to be present; there seems to be a biological side of the association that goes through pregnancy and childbirth, changing the lipid profile and carbohydrate metabolism, and over time this might lead to CHD risk, and ultimately events. This association seems to be confounded as well by SES and in particular education and mediated by the sedentary life style some women were leading. Central obesity which is a major component of the metabolic syndrome seems to exert a large effect, as a high percentage of women had central obesity. This could in part translate the higher rate of the metabolic syndrome among these women especially those with high parity. Therefore the biological association is there at least for some of the outcome variables, yet there is other mechanisms that could influence this association such as socio-demographic or lifestyle factors in response to pregnancy and/ or the raising of children.

6. Consideration of Alternative explanations:

It is always crucial to look at other possible explanations (mainly, confounders) and rule them out before making conclusions about a causal relationship between an exposure and an outcome. For example what else, other than a real effect of parity on risk of developing CHD could explain the results of this study? So confounders give the main alternatives. For example, high parity women tend to be older and CHD risk rises with age. Another example, women of higher social standing may tend to have fewer children and also to have less CHD risk. Women of higher parity tend to be physically inactive and CHD risk rises with less physical activity and sedentary life style. Adjustment for confounding is meant to allow for this, but the adjustment is never perfect and for some possible confounders, such as social standing, we don't have direct measures so we use proxies such as education. It is always possible that the association is due to unmeasured or residual confounders that we could not control for in our analysis.

7. Appropriate design:

A cross sectional design is not ideal for capturing time related causation. This study is observational rather than experimental and it would not be possible to randomize parity. So this issue cannot be addressed in terms of design, and it remains a weakness.

8. Specificity:

The effect of parity cannot be specific in the sense of being a single cause. There are a number of risk factors of which parity is only one, and many of which are also correlated with parity. This study cannot satisfy this criterion.

9. Coherence:

The results of this study are coherent with those of other studies examining the association between parity and CHD risk factors among women. The results of the study suggest that childbearing in addition to life style factors, physical inactivity and leading sedentary habits contributes to CHD risk factors in this group of women. Therefore the association could be due to the biological consequences of pregnancy and sedentary lifestyle.

14.2 Parity and CHD Risk Factors

14.2.1 Parity and Obesity

In this section, we look in more detail at the hypothesis that an increasing number of children is associated with an increasing risk of obesity. What is the extent of this relationship and what are the pathways that lead to parity-related obesity among Palestinian refugee women? Can the same mechanisms found in developed countries be applied to less developed countries such as Palestine where women are overweight and have different childbearing patterns (short birth intervals and multiple pregnancies) and lifestyles?

14.2.1.1 BMI as a Measure of Overall Obesity *(Hypothesis 1)*

The prevalence of obesity represented by BMI ≥ 30 kg/m^2 was positively associated with increasing parity and gravidity, current unemployment, physical inactivity,

having assistance with housework, elevated triglyceride level and DBP and SBP, as well as with central and abdominal obesity. On the other hand, the prevalence of obesity appeared to be negatively associated with the educational level of women and their husbands, and the HDL-C level.

Women with higher parity tended to be older and less educated and their husbands also tended to have low levels of educational attainment. Nevertheless, an association between increasing parity and obesity adjusted for these confounders (age, educational levels, and marital status) was still evident. The results show a 14% increase (CI: 1.07 to 1.22, p <0.0001) in odds of obesity for each additional child after adjustment for age, marital status and educational level of the woman and her husband. Similarly the regression coefficient of BMI increased by 0.28 kg/m^2 per extra child, (CI: 0.15 to 0.42, p<0.0001) and adjustment for the confounders (age, marital status and educational level of the woman and her husband) did not reduce the magnitude of the association.

Adjustment for other predictors of obesity that might act along the causal pathway between parity and BMI, such as lifestyle factors (physical activity, hours per week watching TV and assistance in housework) and reproductive health variables (age at menarche, age at menopause, menopausal status, use of oral contraceptive pills) did not reduce the magnitude of the association, with the exception of assistance in housework, though the association with parity remained significant, as shown in Table 8-5. Assistance in housework decreased the regression coefficient for the association of BMI on parity noticeably, suggesting that some of the influence of parity on BMI is mediated by assistance in housework. Assuming that such assistance results in a more sedentary lifestyle (see above), the fact of leading this sedentary life is partially influenced by parity since this assistance is more common among the higher parity women. Reverse causality might apply here, for example because these women are obese as a result of having many children, they tended to seek assistance in households from their daughters.

Findings in relation to existing literature: The results of this study were consistent with previous studies that examined the association between parity and BMI among women who have completed their childbearing years. Weng et al [126] found a 7% increase in risk of obesity for each additional child after adjusting for confounders,

while Bastian et al [154], found an 11% increase in risk of obesity with each additional child that was independent of socioeconomic status and other confounders. Both studies used data from the Utah population where the majority was Mormon and women bore many children. The number of live births per woman ranged from 0-14, with a mean of 4 live births, which although high is still considerably less than the mean for live births in this study (7.3). In this study, there was a 14% increase in risk of obesity with each additional child after adjusting for confounders, which is larger than other studies.

Our results also agree with those from the Finnish study by Helovaara and Aromaa [136] that looked at the association between parity and obesity among women aged 25 to 84 years. They found that women with 10 or more childbirths were on average 2.3 kg/m^2 heavier than women with no births. They also showed independent effects of age and parity on obesity. Our study found similar associations, where the mean BMI increases by 0.28 kg/m^2 per extra child, and also independent effects of age and parity on obesity.

The consistency of these results concerning parity with ours is important as strengthening the evidence of genuine associations; this is particularly true in view of the many statistical tests involved in our analysis.

14.2.1.2 WC as a measure of central obesity (Hypothesis 2) and W/H ratio as a measure of abdominal obesity *(Hypothesis 3)*

1) WC as a measure of central obesity: While the relationship between parity and BMI has received much attention, relationships between parity and other measures of adiposity such as fat distribution have remained relatively unexplored. This study examined the association between parity and central obesity measured by waist circumference (WC $\geq$ 88 cm). In this study, waist circumference $\geq$ 88 cm was significantly and positively associated with increasing parity, increasing gravidity, increasing age, marital status, currently unemployed, early age at first marriage, early age at first birth, menopausal status, elevated cholesterol, LDL-C, TG, DBP and SBP, hypertension, diabetes, increased BMI and W/H ratio. WC $\geq$ 88 was also significantly and inversely associated with the educational level of the women and their husbands, availability of assistance in housework and HDL-C level. The same

statistical models used with BMI were applied to assess the association between parity and WC.

The mean WC and the prevalence of central obesity (WC ≥ 88 cm) increased significantly with increasing parity. Adjustment for age, educational level of the women and their husbands, and marital status reduced the magnitude of the trend slightly but it remained significant. The unadjusted odds of central obesity (WC ≥ 88 cm) increased by 18% with each additional child. Adjustment for age and educational level reduced this gradient of risk to 16% and 15% respectively. With marital status added to the model, the risk of central obesity increased by 18% with each additional child.

When parity was measured on a continuous scale and using ordinary regression, the mean WC increased by 0.69 cm per extra child. Adjusted for confounders, the magnitude of change was reduced to 0.58 cm but the association remained significant.

Adjustment for most other predictors of central obesity that might act along the causal pathway did not reduce the magnitude of the association. These results show that none of the socio-economic status factors, behavioural and reproductive health factors could explain the association between parity and WC. However, when the assistance in housework variable was introduced into the regression model, the regression coefficient of WC on parity decreased noticeably compared to the effect of the other mediators. The slope of WC on parity was reduced from 0.58 to 0.43 cm per each additional child, suggesting that some of the influence between WC and parity is mediated partially by assistance in housework. The way this mediator might act as a correlate of sedentary lifestyle is discussed above. Although assistance in housework seems to carry some of the influence of parity on WC, the association between WC and parity remained significant. This suggests that the association could be due to the biological consequences both of pregnancy and of sedentary lifestyle.

2) W/H ratio as a measure of abdominal obesity: Another measure of body fat distribution is abdominal adiposity, defined as waist to hip ratio (W/H ratio ≥ 0.85). This indicator was positively and significantly associated with age, marital status, menopausal status, use of contraceptive pills, obesity and central adiposity, TG, T-CHOL/HDL-C ratio, SBP, DBP, hypertension and diabetes. It was negatively and

significantly associated with women's education and HDL-C levels. However, no association was found with parity before or after adjustment for socio-economic factors. The relationship between parity and W/H ratio remained not significant.

In the absence of evidence of an association between parity and W/H ratio, the effects of mediators were not investigated.

Findings in relation to existing literature: Tonkelaar et al [144] found an association between parity and W/H ratio but the strength of the association diminished with increasing BMI. They also found that the clearest association between parity and W/H ratio was seen in non-overweight women [144]. Abdominal obesity as shown by W/H ratio (≥ 0.85) is an indirect measure that predicts insulin resistance (hyperinsulinemia), although many studies do not show a strong relationship between central adiposity (WC ≥ 88) and insulin resistance, perhaps because of the inclusion of only very obese subjects (there is a plateau in insulin resistance above a BMI ≥ 30), or because of the use of indirect methods to measure abdominal adiposity and/or insulin resistance [268]. Results of the study here have shown that the majority of women were obese with higher rates of central and abdominal obesity and that might explain the plateau in insulin resistance. In our study the majority of women presented with central and abdominal obesity as well as overall obesity, yet while there was an association between parity and BMI ≥ 30 kg/m^2, on the one hand, and between parity and WC ≥ 88 cm, on the other, no significant association was found between parity and W/H ratio ≥ 0.85 cm.

It is important to note that most of the studies exploring the association between parity and central adiposity were of pregnant women or women of childbearing age [120] [90, 147]. No studies were found that looked at WC changes associated with parity among older women. Although WC was measured in all of the studies of pregnant and childbearing-age women or older women, it was measured within the context of W/H ratio. Studies of pregnant and childbearing age women that explored the association between parity and central obesity have shown WC to increase with increasing parity.

Interpreting the associations found between parity and BMI and WC in terms of causality is difficult in a cross-sectional study, but the high and independent associations observed in this study speak in favour of a causal relation. There might be other biological mechanisms that could be causal and in part explain this relationship. For example, certain sex hormones or other internal or external factors might both determine the distribution of adipose tissue and the degree of adiposity.

The persistent relationship between parity and BMI and WC despite controlling for socio-economic factors, lifestyle risk factors and reproductive health factors is a finding that needs further exploration among Palestinian women in urban and rural areas and possibly among a larger sample of refugee women. Further studies might be needed to explore additional mechanisms and use more accurate measurements of mediators.

The next sections look at the confounders and mediators, and at issues of causality, for these relationships in more detail

14.2.1.3 Parity, Obesity and Socio-Demographic Factors

Age: Both parity and the prevalence of obesity are age dependent. Parity increases with increasing age and obesity increases with increasing age, yet both were correlated independently of age. The results showed slight age confounding but this had only a small effect on the magnitude of the association.

The study showed parity increasing with increasing age. Older women tended to have more children than younger women in spite of the fact that all women participating had finished their child bearing. This probably reflects the fall in total fertility in recent years. One notes that in some studies, the association between obesity and age was explained in part by a decrease in the degree of physical activity with age among women [261, 269]. This does not seem to be the case here since activity levels were low for all age groups, although it is possible that the fact that physical activity was not measured exhaustively did not allow this to be seen clearly enough.

Educational levels: Several investigators have found that educational level confounds the relationships between high parity, early age at first live birth and risk for obesity [94]. Women with less education may be poorer and at higher risk for obesity because of their health behaviours (excessive caloric intake and less physical

activity). In this population of older women, education was inversely associated with obesity. Women in the camps are less likely to attain a higher education in view of early marriage and reproduction. This in turn makes obtaining a job more difficult for these women, since they become occupied with the care of a larger number of children. When husband's years of schooling was used as a proxy to socio-economic status there was little variation found between families.

Marital status: The influence of marital status is probably related to age and parity since marriage traditionally takes place at a relatively young age and reproduction is encouraged in the refugee camps. Marital status is also related to obesity; one study found the prevalence of obesity to be higher in widowed and married women than in single women [270]. The large majority of women in this study were found to be married so power to detect effects of marital status was limited.

These reasons give background to the findings that the above socio-demographic variables did not appear much to confound associations between parity and BMI and WC.

14.2.1.4 Parity, Obesity and Physical Activity

Physical activity has been reported as a determinant of body weight [107, 145]. Our findings show that it is an important correlate of BMI and WC in these women, but does not reduce the magnitude of association between parity and obesity. Other variables such as assistance in housework which seems to be a proxy for less physical activity and was associated with parity reduced the magnitude of the association, although it remained quite significant.

This could be explained by the fact that the refugee camps in Palestine are socially different from Western countries. There are limited outdoor sport and leisure activities, especially for women, and little media reinforcement of healthy body weight. The social and cultural environment does not encourage women to think about weight reduction. Moreover, traditional Arab culture does not consider obesity per se to be a sign of bad health; it is often considered a sign of beauty, wealth and good health. The lack of employment opportunities outside the home may also contribute to the higher frequency of obesity among Palestinian women.

The concept of leisure time physical activity is not a common one in the Palestinian context, especially for refugee women, where lack of facilities for women and cultural norms are prohibiting factors. Three questions were used in the analysis to reflect whether women practice any type of physical activity (yes or no), kind of physical activity and the number of hours practiced per week. The 69 women in the sample who engaged in physical leisure activity reported that it was restricted to walking for an average of 3 hours per week. More sensitive instruments are clearly needed to evaluate the physical activity of this largely sedentary group. Imprecise measurement of physical activity may lead to inadequate control for it which in turn may lead to residual confounding.

Assistance in the home is usually given by older daughters, which is more common in higher parity women. This factor could also create differences in activity levels between women who have assistance and those who do not. In view of the results of these analyses, it may reflect activity levels more effectively than responses directly about activity.

14.2.1.5 Parity, Obesity and Reproductive Health Factors

Lifestyle risk factors and other reproductive factors such as age at menarche, age at menopause, age at first birth and use of oral contraceptive pills, have been reported to be related to obesity. However, the association between parity and BMI was not reduced after adjustment for these variables.

Younger age at menarche was associated with increased BMI among these older women. This result is consistent with Bastian et al [106] who found the same phenomenon among older women, as well as Symons et al who showed body composition measures (percent of lean mass) are linked to the timing of menarche and menstrual cycle length [271]. Women are also prone to weight gain during menopause. The loss of the menstrual cycle affects calorific intake and slightly lowers metabolic consumption, although most weight gain here has been attributed to a reduction in physical activity.

Pregnancy may affect the risk of obesity through insulin resistance. Insulin resistance is greater in multigravid women than in women with fewer pregnancies, perhaps as a

result of altered glucose metabolism during pregnancy or post-pregnancy alterations in the amount and distribution of body fat [122]. Grand multiparity had a highly significant effect on BMI. This is probably related to weight gain during repeated short-interval pregnancies that do not allow for enough weight loss [136].

Various studies which considered the number of pregnancies have included spontaneous abortions. However, biological effects can be more prominent in full term pregnancies (mainly with live births) in comparison to short term spontaneous abortions, if we consider that the biological mechanism mediating the relationship between pregnancy and obesity is hormone or insulin resistance related. Although the association between gravidity and parity is high, the two factors may not be compatible if pregnancy losses affect obesity risk. In this study, the number of pregnancies was also related to obesity (data not shown).

Another main influence on obesity is the effect of parity on the number of ovulatory cycles since more pregnancies imply fewer cycles and in consequence less of the linked hormonal alterations, with such as a decrease in endogenous oestrogen causing an increase in BMI and obesity, and changes in body fat distribution [244]. Hence, an independent effect of oral contraceptive use is expected, because oral contraceptives function by inhibiting ovulation. In this study, we observed a higher rate of oral contraceptive use in obese women compared to non-obese women. Oral contraceptive users were found more among women with higher parity. Use of oral contraceptive pills is socially and religiously allowed to space children, but not to prevent having children, unless there is a medical reason to prevent further pregnancies. Only 40% of women ever used CPs; the majority of women preferred to use the IUD.

Another potential mechanism for the development of obesity is that pregnancy and child rearing have an impact on levels of stress and social support. Stress has been shown to lead to poor health outcomes, but higher social support may counteract the effect of stress [10]. Although social support was not measured in our study, stress was measured and a positive association with parity was found. However, no significant relationship between stress and BMI was found.

Further analysis between parity and obesity was adjusted by physical activity, hours watching TV and assistance in housework as a proxy to physical activity, as well as

plasma insulin. None of these factors mediated the association between parity and obesity, except assistance in housework reduced the magnitude of the association and could partially reduce the effect of parity on BMI. As has been indicated, this could imply that a sedentary life style might add to the relationship between parity and obesity. Plasma insulin was also adjusted for, but did not reduce the magnitude of the association of parity and obesity. Insulin levels did not differ markedly among the different parity groups.

14.2.1.6 Public health implications relevant to obesity prevention, health policies and programmes

The results of this study indicate the prevalence of obesity and high WC among women aged 40-65 with the maximum rate among the most multiparous women. What kind of health policies are needed to prevent or reduce this increase of obesity in Palestine?

The first point to note is that fertility is declining in this population which, in itself, can be expected to impact favourably on obesity and overweight. However, further consideration needs to be given as to how to reduce the impact of pregnancy and childbearing on obesity.

Immediate attention should be given to the management of female overweight, obesity and central adiposity in the refugee camps of Palestine as an increasingly serious public health problem and a risk factor for many chronic diseases that develop later in life. Quality improvement is necessary in the pre-natal programmes currently implemented at the public health centres, especially concerning nutritional guidelines.

The results of this study suggest the need for the development and implementation of programmes to prevent and treat the problem of parity-related overweight and obesity. Such programmes could help women avoid excessive gestational weight gain through each pregnancy and birth and encourage postpartum weight loss by promoting dietary changes and physical activity alongside exclusive breastfeeding. They should be targeted at young women, women of childbearing age and beyond childbearing age. Interventions to reduce and prevent obesity should also target women who are overweight prior to their initiation of childbearing.

Policies should be supported by effective research. More studies are needed to examine determinants of excessive weight gain and postpartum weight retention and its effect on body fat distribution among women in later years after childbearing. However, with the rising prevalence of obesity among women of childbearing age and after childbearing age and the high proportion of women who are gaining excess weight, a shift in research and services focus must occur to include consideration of the mother's long term health status in addition to the child's health status. Long term studies to identify the relationship between parity and obesity are needed as well. The impact of excess WC gain associated with childbearing on women's future health risk should be evaluated further.

14.2.1.7 Study limitations relevant to parity and obesity

The present study controlled for a number of variables that might be expected to influence weight gain, such as behavioural factors and in particular physical activity. There are other factors that were not included in this analysis that may account for some of the differences in weight gain among the parity groups such as maternal weight gain during pregnancy and food intake.

The basic concept underlying interpretation of these results is that pregnancy or repeated pregnancy (or births) changes the physiology in a woman's body, possibly making her more prone to diseases including heart disease. Correcting completely for confounders is desirable but seldom possible.

Zero parity is used in many studies as the baseline comparison group, in order to detect where the change occurs and at what parity level effects can be seen. However the zero parity group is numerically few, and is culturally and physiologically unique in this community and differs from the same group in other parts of the world where many women are voluntarily childless, so where not having children can be a more specific choice. Non-gravid women here may differ in other respects that were not measured in this study. Here many of the women who remain nulliparous may be subject to couple infertility or to hormonal disorders affecting fertility. Aside from their uniqueness, more comparisons with the zero parity group was not possible since this group was so small.

Due to the political situation at the time of data collection, and due to financial constraints, the study could not be expanded to include more than two refugee camps. Including additional camps and also increasing the sample size would have increased the number of women in the zero parity group and the statistical power to detect associations by comparing to this group.

Another limitation is possible error in the women's statements of their age at menarche, age at menopause, number of abortions/miscarriages, and number of still births the woman had throughout her life. This is due to inaccurate recall among some women of events that occurred in the distant past. We have focused on live births because pregnancy losses are less likely to be fully recalled than the number of live births. Many pregnancy losses are clinically unrecognized and therefore not recalled. Additionally, women may have reported physical activity and smoking behaviours inaccurately because of social norms.

It remained unclear whether the association between the number of children and obesity is primarily mediated though biological or behavioural mechanisms or both. One of the drawbacks of this study is that men were not included. Inclusion of men could have helped to identify associations mediated through behavioural (lifestyle risk factors associated with having large families) or biological mechanisms, though only partly because of different lifestyle norms for fathers and mothers.

Finally, a theme that recurs throughout this work is that many comparisons and statistical tests are made. The chance of an erroneous positive finding is increased. Comparison of the results of this study with finings in the literature is an important check here.

14.2.2 Parity and Hyperlipidemia *(Hypothesis 4)*

The relationship between an increasing number of children and the risk of elevated lipids and lipoproteins was examined. No association was observed between parity and elevated total cholesterol, LDL-C and HDL-C in this sample of women. An apparent association between triglycerides and parity was observed when both were measured on a continuous scale. The mean TG increased by 0.038 mmol/L (3.4 mg/dl) per extra child, p= 0.003. Adjustment for age, the woman's education and husband's years of schooling, and marital status slightly reduced the magnitude of

change in mean TG, but the association remained significant, p=0.03. This degree of significance was not strong so caution is needed because of the multiple testing problem. But if it is accepted, then confounders could not fully explain the association between triglycerides and parity. Assistance in housework, waist circumference, BMI, diabetes and to a lesser extent W/H ratio partially mediated the association between parity and triglycerides. BMI and assistance in housework seemed to have the strongest mediating effect.

An apparent association between T-CHOL/ HDL-C ratio and parity was observed when both variables were measured on a continuous scale. The unadjusted mean T-CHOL/ HDL-C increased by 0.001 mmol/L (0.05 mg/dl) per extra child, p=0.020. This association was attenuated after adjustment for age, and was completely abolished after adjustment for women's educational level, husband's years of schooling and marital status as in Table 9-17.

The results of this study cautiously suggest that of all the lipid and lipoprotein variables, triglycerides may have been associated with parity. Increased triglycerides levels in women with more children appeared to be mediated by greater obesity represented by BMI and sedentary lifestyle represented by assistance in housework. These results suggest that the relationship between parity and triglycerides levels could be associated with either the long term biological consequences of pregnancy through the alterations of lipid levels and/or the weight increase associated with pregnancy or the women's sedentary life style and the stress of childbearing.

Most of the studies reviewed focused on HDL-C levels as being the most powerful predictor among all the lipids and lipoproteins in determining cardiovascular diseases in women [252] [82]. Furthermore, in the few studies available on the long term effects of pregnancy on lipid and lipoprotein levels, there has been agreement that multigravid/multiparous women have lower HDL-C levels than nulligravid/ nulliparous women. The magnitude of the effect has been shown across various studies to be of the order 0.03 mmol/L (1 mg/dl) and to decrease with each pregnancy or birth, after controlling for the effect of confounders and correlates such as age, smoking, alcohol use, physical activity, oral contraceptive use, education and marital status. However, there has been disagreement about the linearity of the association among these studies, as can be seen in the literature review on parity and lipids.

Our results confirm a trend of decreased HDL-C with increasing parity groups, starting from parity 1-3, but the trend did not attain significant levels. We also found age-adjusted HDL-C levels decreased, but by 0.007 mmol/L per extra child (coefficient = -0.007 with 95% CI: -0.014 to 0.00008, p=0.053), which is significantly less that the 0.03 mmol/L quoted above. Adjustment for educational level attenuated the association and it became no more significant.

The small sample size of the study may have contributed to not finding an association; nevertheless the fact that the coefficient was low should be noted. Lawlor et al found that the number of children among British women and men participating in the British Women's Heart and Health Study and the British regional Heart Study, was inversely associated with high density lipoprotein cholesterol and was positively associated with triglycerides and diabetes [2]. The sample size used by Lawlor of 3828 women was large enough to detect an association of less magnitude. The same applies to Kritz-Silverstein et al, where they found women with 5 or more pregnancies had significantly lower levels of HDL-C before and after adjustment for age, obesity, diabetes, alcohol and cigarette consumption, exercise and estrogen use using a sample size of 1275 women, but the association was not linear as in Lawlor et al. [123].

Our finding of a significant, though not strongly significant, association between parity and triglyceride levels is consistent with Lawlor's et al study where the number of children was found to be significantly associated with higher triglycerides levels, and that each additional child increased the age-adjusted mean triglycerides by 0.02 mmol/L, (95% CI: 0.01 to 0.03, p= 0.001).[2] In our study (data not shown), each additional child increases the age-adjusted mean triglycerides levels by 3.3 mg/dl, (95% CI: 1.00 to 5.64, p= 0.005), which is equivalent to 0.04 mmol/L, (95% CI: 0.01 to 0.06), whereas Kritz-Silverstein et al found no statistically significant differences in levels of triglycerides between nulliparous and parous women.[123].

Another way in which my study also differs from others is that not all of the women involved in the study were postmenopausal. Women have completed their childbearing, but some of the women in their 40s and 50s were still pre-menopausal, and at less risk for some of the diseases and disorders that I was studying (especially heart disease-CHD- and cholesterol differences). That could be part of the reason why I don't observe some differences in cholesterol. It could also mean that my results are

more conservative, in other words, if I have concentrated on older post menopausal women who lose the protection from heart disease that women have until menopause, I might have found stronger relationships.

Results of our study have shown a tendency for triglycerides levels and Chol/HDL-C ratio to increase with increasing parity, starting from parity 1-3 (section 7.7). Furthermore triglycerides levels increased significantly among women who were unemployed, physically inactive, ever used OC pill, less educated, diabetic and had elevated BMI, WC and W/H ratio, as well as a positive family history of diabetes. Women who were obese and had more central and abdominal adiposity or who were diabetic had higher levels of triglycerides. At the same time women with many children tended to be less educated, unemployed, leading a more stressful life, had higher BMI and WC and higher rate of ever use of the contraceptive pill.

So we consider that any association between parity and triglycerides could be partially explained by obesity and central obesity which in turn are likely to be consequences of higher parity, assistance in house work as a proxy to physical inactivity and being diabetic, as these covariates tended to mediate the association between parity and triglycerides. Both obesity and assistance in housework as a proxy to physical inactivity were at higher levels among women who have more children. Palestinian women in the refugee camps tended to get considerable assistance in housework as the elder daughters will look after the young and will do all the housework, and the mothers will lead a sedentary life; this contributes to their elevated BMI and WC and would lead to increased triglycerides levels, whereas in western populations one is less likely to observe daughters or daughters-in-law help in housework.

Findings considered further in relation to the existing literature: It seems the association between parity and elevated lipid levels are more likely to be observed among lean women rather than among obese women. Kritz-Silverstein stated that women in the Rancho Bernardo cohort were on average leaner than other US women and therefore considered that in populations that are less lean than the Rancho Bernardo cohort, the association between parity and high density lipoprotein levels might have been noted with fewer pregnancies, where they found a significant negative and more linear association between parity and high density lipoprotein [123]. In our study we managed to observe a probable association between parity and

triglycerides but we were unable to detect any association with HDL-C level although the trend for decreased HDL-C with increasing parity was present. The association might have existed but either the power of the study was insufficient to detect it or women who were obese and less physically active reduced the effect, and the association could not be seen, alternatives that requires further investigation.

During a healthy pregnancy, the progressive rise in blood insulin and gestational hormones is accompanied by elevations in blood lipids, insulin resistance and weight gain [272]. Whether this association persists years after childbearing has been examined in several studies of both pre- and postmenopausal women [114] [2] [184] [273]. These studies have reported an inverse relationship between parity and HDL-C, and lower HDL-C levels at a threshold of high parity (five or more births vs. four or less births [123] [274]. Van Stiphout found that lower levels of HDL-C persisted up to 6 years after child birth [176]. Kritz-Silverstein observed an inverse association between higher parity and HDL-C 10 or more years after the last pregnancy [123] and Humphries et al provided evidence that lower HDL-C levels following pregnancy persist for decades after childbearing has ceased [114]. In our study we could not identify a significant association with lower HDL-C but a significant association was observed between elevated triglycerides and increasing number of children in this group of women.

14.2.2.1 Public Health Implications Relevant to Hyperlipidemia

Regular check ups and routine examinations of lipid profile should be part of an overall programme for the assessment of risk factors for CHD among women and men in Palestine. This should include awareness programmes for women about the long-term effect of pregnancy and child bearing on women's health and in particular on hyperlipidemia that leads to CHD mortality and morbidity.

14.2.2.2 Study Limitations

This study is cross-sectional and as such might have been affected by several sources of bias that could have influenced the results:

Participation bias: Participation bias would have been an unlikely reason for the observed association between parity and triglycerides levels. The study selected all women in the camps aged 40-65 years and then chose a random sample without

knowing the number of children borne by women or whether or not they have elevated lipid levels.

Reverse causality: It seems unlikely that elevated triglycerides could lead to an increased number of children.

Survival bias: It is unlikely that the association between parity and elevated triglycerides was due to survival bias; women with a greater number of children dying prematurely of elevated triglycerides would lead to underestimation of the strength of association between number of children and triglycerides levels.

Inclusion of women who were taking medication for diabetes and hypertension and lipid-lowering drugs in the analysis might have masked the association between parity and the mentioned outcome variables. However, it is unlikely that happened since we found women on medication had more elevated lipids, fasting blood sugar and hypertension than those who were not on medication; also these women had the highest parity. This would be consistent with low levels of drug adherence. The results of the analysis excluding those on medication were the same; therefore we decided not to exclude these women from the analysis as presented.

Measurement errors of the confounders and other covariates: The distribution of several known risk factors such as age, education for both women and their husbands, physical activity, assistance in housework and other covariates varied by parity. These factors are therefore potential confounders or mediators of the association between parity and lipid levels. Although these factors were controlled in our analysis, residual confounding due to imprecise measurement of the confounders may still be present. In addition, measurements taken at the time the study was conducted might not reflect exposure levels during childbearing years.

Measurement errors of the outcome variables: Women with elevated lipids were confirmed in the laboratory and therefore the chance of having the elevated lipid levels or not having elevated lipid levels is minimized. Yet there might be other measurement errors in the laboratory, but that was also unlikely since a sub sample was sent to another laboratory for validation of the results.

Exposure information obtained through self-reporting can be susceptible to systematic error. Parity, gravidity and several other variables were reported by the women. Women might have reported parity much better than gravidity as gravidity includes number of still births and number of miscarriages/abortions (see above). However, there is no reason why women with elevated lipid levels would report parity differently from those with normal lipid levels. The same principle applies to type II diabetes mellitus and all outcome variables.

14.2.3 Parity and Type II Diabetes Mellitus *(Hypothesis 5)*

The objective of this section was to examine the independent relation of parity to type II diabetes mellitus in this sample of 40-65 years-old Palestinian women living in refugee camps. The literature reviewed has shown that higher parity is unlikely to have an important impact on the development of type II diabetes in the US and other industrialized countries where few women have more than six children. Exposure to high parity may be relevant, however, in developing countries such as in the Middle East, South America and Africa, where many more women bear 6 or more children. Other studies including parity and the development of type II diabetes mellitus in women have not been carried out in the Middle East. This study represents the first investigation in the Middle East of the association between parity and the risk of developing type II diabetes, in this case among Palestinian women, a population who bear many children and among whom type II diabetes mellitus is on the rise.

In this cross-sectional study no association was observed between parity and type II diabetes mellitus after adjustment for age. The results showed a slight statistically significant increase in the unadjusted risk of diabetes with increasing parity but this increase was reduced and became not significant after adjustment for age. Adjustment for other variables such as education of both women and their husbands and marital status did not have any effect on the association between parity and diabetes. The association between parity and diabetes seems to be explained by age. Parity increased significantly with increasing age and the risk of diabetes increased significantly with increasing age, but age seemed to have a much stronger effect on the development of diabetes than parity.

The adjusted analysis of fasting blood sugar (FBS) taken quantitatively, instead of diabetes, indicated by raised FBS, on a continuous scale with parity also did not suggest any evidence of association. However, one observes in Table 10-2 (Mean values of selected characteristics associated with diabetes among Palestinian women) that there appears to be an association with gravidity. This is not the case for the other metabolic outcome measurements: total cholesterol, LDL-C, HDL-C, and total cholesterol/HDL-C ratio. Triglyceride was the exception, as it showed an association with gravidity as well as with parity. This relationship was pursued further. However; the process here consisted of further analysis based on a hypothesis generated from the same data, against a background of many statistical tests being carried out; therefore conclusions about associations must be viewed as speculative.

As a first stage of this analysis, the association of FBS with failed pregnancies (the difference between gravidity and parity) was examined. No other significant relationship was found to failed pregnancies except for triglycerides, p= 0.028. When fasting blood sugar was regressed in the fully adjusted model, allowing for censoring among those on medication, on the number of failed pregnancies and parity (live births) in the same model, the adjusted coefficient for parity was 0.07 mmol/L, p=0.191, and not significant, whereas that for failed pregnancies was 0.29 mmol/L, and statistically significant (p= 0.001).

The relationship between fasting blood sugar and gravidity was next examined with both variables being continuous, using ordinary regression as in Table 10-6. An apparent significant association between gravidity and type 2 diabetes was observed in the unadjusted analysis. The unadjusted regression slope was 0.15 mmol/L, denoting the predicted rise in fasting blood sugar for a unit rise in gravidity, (95% CI: 0.08 to 0.22, p <0.0001). Adjustment for age, women's education, husband's education and marital status reduced the magnitude of the association but it remained significant. So confounders could not fully explain this apparent association between gravidity and type II diabetes.

Failed pregnancies seem to have the highest mediating effect amongst all mediating variables, reducing the magnitude of the association with gravidity to a great extent. This is to be expected, as failed pregnancies are the component of gravidity that most

predicts FBS. This confirms that the association between gravidity and type II diabetes goes through failed pregnancies.

WC and the W/H ratio also noticeably reduced the magnitude of the association between gravidity and type II diabetes, which indicates that these variables exert a partial mediating effect. It has been well documented in the epidemiological studies that central and abdominal obesity predict type II diabetes among both men and women [275], and that abdominally localized obesity is particularly strongly associated with increased risk of developing diabetes. The strongest risk factors for the development of type II diabetes in addition to abdominal obesity were low sex hormones concentrations and high fasting plasma insulin as cited in the literature. This suggests that abdominal obesity is linked to insulin resistance, one of the major factors in the development of diabetes mellitus [275]. In addition to that, the WC and W/H ratio seems to be associated with a cluster of the metabolic risk factors as well as hypertension [275]. It has been documented that abdominal obesity measured by the W/H ratio may be an important risk factor for diabetes in rural Palestine as a result of the socioeconomic changes and increasing urbanization Palestine is undergoing [276]. Results from our study suggests that WC and W/H ratio were strong predictors for developing diabetes mellitus among women, but failed to show that they act as mediators in the relationship between parity and diabetes, since we found no association with parity in the first place. But, for the analysis involving gravidity, the mediating effect of W/H ratio and WC was apparent. Our study found also that the degree of central and abdominal obesity was significantly related to number of children and other variables of reproductive history.

The results of our study, showing no evidence of an association in an adjusted model, between parity and type II diabetes, are consistent with a previous study that controlled for age, BMI, educational level, and socio-economic status [197], and with another study that controlled for age and BMI and conducted in a relatively homogenous population [196]. In both studies no evidence was found of an independent association between parity and the development of type II diabetes mellitus.

Other studies have demonstrated both higher parity and diabetes to be associated with lower educational attainment and lower socio-economic status and these could be important confounders for the association between parity and diabetes [194] Women in our study also showed lower educational attainment and lower socio-economic status with increasing parity. Yet confounders including age, women's education, husbands' education and marital status could not explain the significant association between gravidity and type II diabetes mellitus.

There have been many inconsistencies in the literature regarding the relationship between parity/gravidity and type II diabetes. Earlier studies suggested that parity, particularly five or more births, might be associated with diabetes [192] [122] [187], whereas other investigators have found no association [194, 196, 197] Potential mechanisms include the influence of multiple pregnancies on postpartum weight retention [153]-[277] and development of obesity [167, 194, 197] or the influence of multiple exposures to the metabolic changes of pregnancy [192], including impaired insulin sensitivity and central obesity [278]. Other studies [187, 273] [279] suggest that nulliparity (no live births) may be associated with diabetes. Potential mechanisms include underlying insulin resistance and B cell dysfunction [187] related to infertility and pregnancy loss [280].

There are a number of factors that might have influenced the results in this case. The finding here that gravidity rather than parity, and incomplete pregnancies even more so, are definite correlates of FBS remains somewhat puzzling. The missing element in comparing gravidity and parity is that of the remaining gestation, cut short, and the post-partum period which includes breastfeeding, fairly universal in these women. Details of gestation at the time of pregnancy loss are not available, and it is hard to make more progress in deduction of factors likely to matter here. One must bear in mind that this is an additional analysis so the scope for chance effects is greater. Nevertheless, the effect of failed pregnancies was strongly significant, at $p=0.001$.

Inclusion of women who are taking medication might have masked an underlying association between parity and diabetes. However, the study found higher FBS among those that reported they were taking the medication compared to those who said they were not. We also found that women who said they were on medication tended to be

in the high parity group and have the higher FBS. Furthermore, the use of censored regression models did not change the basic conclusions.

Our study has shown that the mean number of children was not significantly higher among women who were diagnosed as diabetic compared with women who had normal glucose tolerance (7.8 vs. 7.2 children, p=0.108). This result is in agreement with a US survey on women aged 55 to 74 years of age, where the mean number of children was slightly higher among women with diagnosed diabetes than among women with normal glucose tolerance (3.4 vs. 2.7 children) [122]. On the other hand, women with high fasting blood sugar were older and women with high parity/gravidity were also older; this suggests that the removal of the effect by age confounding is needed here also. Whether the process of becoming pregnant and having more children might lead to diabetes or whether the association is due to age effects was investigated. In our study the age effect component was apparent in the association between parity and type II diabetes, and while age confounded this association, it could not fully explain the gravidity and fasting blood sugar relationship as the association remained significant even after adjustment for age.

The finding of a relationship between FBS and gravidity but not parity is not in agreement with the Rancho Bernardo study where similar patterns of association were found between the two exposures (parity and gravidity) and risk of diabetes [122]. That study was larger (1186 women) but had fewer women at the upper levels of parity and gravidity.

Reported family history of diabetes did not seem to modify the association between gravidity and diabetes mellitus, although women reporting a family history of diabetes were at increased risk of developing type 2 diabetes compared to those without a family history. This result does indicate that diabetes mellitus has a hereditary component; in agreement with Kritz-Silverstien of the Rancho Bernardo study in the US where they found women with a family history of diabetes had more than twice the risk of having non insulin dependent diabetes mellitus as those without such a family history [122].

The study results give no evidence that parity influences diabetes, so it is uncertain whether increasing parity may influence the later development of type II diabetes in

the susceptible group of women with gestational diabetes. One study demonstrated that women who have had gestational diabetes are at high risk of future diabetes. That study found that each additional pregnancy after an episode of gestational diabetes (GDM) further increased the likelihood of subsequent diabetes by 3.34 times compared to women who did not have a further pregnancy [281]. In our study we were not able to analyze the data for women who reported to have gestational diabetes because they constituted a small number (4%) of the sample and therefore the statistical power of any analysis would be low.

There are several possible mechanisms to explain an association between parity and type II diabetes.

- Women with higher parity might have a higher caloric intake and lower physical activity than women with lower parity. Sedentary lifestyle behaviour could lead to higher BMI, insulin resistance and development of diabetes [280, 282]. Results from our study showed that women with higher parity had a higher BMI, central and abdominal obesity than women with lower parity, and therefore postpartum weight retention with multiple births coupled with a sedentary lifestyle might lead to the development of diabetes. All that has been stated above applies to this study, yet we did not find an association between parity and type II diabetes, although there was clear association between gravidity and type II diabetes. This may be an issue of statistical power for the relationship with parity; the sample size in the present study was not large, but the contrast with the relationship with gravidity remains something of an enigma, as we saw above.

- While some investigators propose that hormone levels might heighten insulin resistance [283], others suggest that hormones might adversely affect insulin resistance and increase the risk of diabetes. Our findings did not support any effect of menopausal status or oral contraceptive use as potential mediators of the association between parity and diabetes.

In conclusion, despite a diabetogenic effect of pregnancy, we observed no association between parity and later development of diabetes mellitus after adjustment for age among women aged 40-65 years in the refugee camps, although the association exists

between gravidity and development of diabetes mellitus even after adjustment for age and W/H ratio; socioeconomic factors could not explain this association between number of pregnancies and the development of type II diabetes. This association seems to be explained by failed pregnancies and partially by WC and W/H ratio indicating central and abdominal obesity among women.

14.2.3.1 Public Health Implications Relevant to Parity and Type II Diabetes Mellitus

The main implication of our study is that the association of pregnancy with development of type II diabetes whether through biological mechanisms or lifestyle behaviours deserves further study. The findings suggest the need to further explore patterns of postpartum weight retention. To incorporate effective educational initiatives focusing on nutrition and physical activity into prenatal and postnatal care may be a reasonable strategy to promote healthy lifestyle behaviours among women. This work suggests the need for physicians to discuss potential long term effects of pregnancy on health to women and patients who already have diabetes. Multiparous women should be counselled about the increased risk of diabetes especially if other risk factors are present.

14.2.4 Parity and Hypertension *(Hypothesis 6)*

Hypertension has long been recognized as a risk factor for CHD. Does an increasing number of children lead to elevation in diastolic blood pressure (DBP), systolic blood pressure (SBP) and hypertension in this group of women?

The results of previous studies attempting to demonstrate an association between gravidity/parity and hypertension have led to inconsistent results. Our results show an apparent association between parity and SBP in an unadjusted analysis. Adjustment for age and other confounders (women's education, husband's education and marital status) attenuated the association. No evidence was found of an association between DBP and parity.

Women with elevated SBP, elevated DBP and hypertension were significantly older, less physically active, had more central and abdominal obesity and were more often in

the menopausal (post menopausal) state. Furthermore, women with elevated systolic blood pressure tended to be more obese (BMI $\geq$ 30 kg/m^2), diabetic with higher levels of total cholesterol and LDL-C, tended to have more pregnancies that ended as still births and were less educated. All these characteristics were consistent with other studies that investigated the association between these factors and blood pressure among older women.

The positive association between number of children and elevated SBP became non significant after adjustment for age. The change in odds of SBP $\geq$ 140 mmHg or on medication, per extra child (unit change in parity) was 1.06 mmHg (95% CI: 1.01 to 1.11, p=0.027). After adjustment for age, the change in odds of SBP $\geq$ 140 mmHg or on medication per extra child (unit change in parity) became 1.02 mmHg (95% CI: 0.97 to 1.07, p=0.442). The same applies to the association between number of children and unadjusted censored mean for SBP, where the regression coefficient was 0.98 mmHg (95% CI: 0.32 to 1.64, p= 0.004), whereas no linear association was found between numbers of children and mean censored with age adjustment for both systolic and diastolic blood pressure. Difference per increase of one child for SBP was = 0.34, (95% CI: -0.29 to 0.96, p= 0.289) and for DBP was = 0.03 (95% CI: -0.28 to 0.34, p= 0.843).

Findings in relation to existing literature: Most of the studies that examined the association between parity/gravidity and blood pressure did not adjust for age or included women at younger ages. The studies that included older women and adjusted for age, obesity and other covariates could not identify a positive association between parity/ gravidity and blood pressure [201] [2] [114] [113].

Lawlor et al [2] found no linear association between number of children and mean age-adjusted systolic blood pressure or mean age-adjusted diastolic blood pressure with both men and women, not even for women with five or more children. (Difference per increase of one child was for SBP= 0.31 (95% CI: -0.33 to 0.94, p=0.35) and for DBP = 0.05 (95% CI: -0.26 to 0.35, p=0.77). Humphries et al [114] found that the mean age-adjusted systolic and diastolic blood pressure and the prevalence of hypertension did not vary with parity among a group of post-menopausal women aged 55-99 years who participated in the Rotherdam study.

Kritz-Silverstein et al [201] found no association between parity or gravidity and hypertension or blood pressure after controlling for a variety of covariates such as age, obesity, alcohol intake, cigarette smoking and oestrogen use. However the study examined a cross-sectional cohort of older white women aged 50 years and above who were of relatively high socio-economic status and generally of low gravidity. Lee-Feldstein et al [202] found that the blood pressure (SBP or DBP) of white women of high and low stress groups that were identified in terms of socio-economic status was not associated with women's reported number of live births, after adjusting for age, percent overweight, race, and stress effects. Ness et al [215] found a stronger association between gravidity and hypertension or SBP for younger premenopausal women compared to post-menopausal women

Overall obesity, and central and abdominal adiposity are risk factors for elevated SBP and DBP and they are significantly associated in our study (data not shown). However introducing BMI, WC and W/H ratio into the model did not change the non-significant association between DBP, SBP and parity.

14.2.4.1 Study Limitations as related to blood pressure

It is unlikely that the lack of association between number of children and blood pressure observed in this study was due to survival bias whereby women with greater number of children had higher blood pressure but died before the study was conducted. It is also unlikely that medical treatment could bias the association. In our study increased parity was not associated with higher use of antihypertensive medication. Also, excluding women on antihypertensive medications had no impact on the association between parity and blood pressure. In fact, we found that women who have high blood pressure were the women with more children and were the least likely to comply with antihypertensive medication.

Weaknesses of these results include the lack of generalizability; the data were from refugee women only and cross sectional. Although a retrospective history of pregnancy and parity was included, measurements of blood pressure reflect current status only.

Smoking is considered a risk factor to hypertension, but we excluded smoking from the analysis because very few women in the sample smoke. Ness et al [215] found a negative relation of current smoking to blood pressure and hypertension which she attributed to physicians recommending smoking cessation to patients with high blood pressure.

In comparison with other studies, women in this study were more obese, had less educational attainment, were less physically active, were of relatively low socio-economic status and had more children. Whether the same mechanisms found in Western countries apply to these women is still not clear. We found a trend of increasing SBP with increasing parity, but the power of the study was limited and we were not able to detect any significant association between parity and SBP among these older women. Thus, we must remain equivocal about the extent of a parity-blood-pressure association. The fact that there is a parity-obesity link and also one between obesity and blood pressure does, however argue for such an association in these women; the lack of direct evidence for it being due to lack of power.

It is well established that changes in blood pressure may occur during pregnancy, but the relationship between parity/gravidity and blood pressure may be different for younger women who are closer to childbearing or who are still coping with small children compared to older women [201]. In our study all women finished their childbearing years and were aged between 40-65 years which could explain in part why there was no evidence of an association between parity and SBP, DBP and hypertension.

14.3 Parity and Other Outcome Variables

14.3.1 Parity and CHD Reported Events *(Hypothesis 7)*

The association between parity and CHD risk as reported by women was investigated. 7.8% of women reported having had CHD events. CHD was defined as self report of a doctor's diagnosis of myocardial infarction/heart attack, angina, valve problem, or heart failure.

Women with reported CHD were older, less educated, and either widowed or, among those married, the husbands were unemployed. They tended to have more children,

and were menopausal. They had elevated SBP, DBP and hypertension. Although these reports may not be completely reliable, this last finding and the fact that less educated women reported more CHD gives support for reliability.

We observed a marginally significant association between parity in groups and reported CHD events, p=0.043. However, adjustment for age removed this association, and it was no longer significant, p= 0.192.

When parity was fitted into an ordinary regression model as a continuous variable and reported CHD was kept as a categorical variable, the change in the unadjusted odds of CHD events per extra child was also non-significant, at 1.05 (95% CI: 0.96-1.15, p=0.249). Adjustment for age, women's education, husband's years of schooling and marital status slightly reduced the magnitude of the association and it remained non significant

We found no significant association between parity and reported CHD events after adjustment for age. Women who reported to have had a CHD event had more children and were also older than women who reported not having had a CHD event.

As has been suggested, there might be unreliability in women's recall of CHD events. Women might have a recollection of angina and/or chest pain but not interpret it as a CHD event. Usually women do not go for a check up or seek a doctor's advice unless they are very sick, and they might have misinterpreted the meaning of symptoms unless they sought advice from a health professional. In a regression model, reported CHD events were significantly associated with elevated SBP, hypertension and elevated W/H ratio.

There have been conflicting findings among other studies regarding the positive association between increasing number of children and the development of CHD events in women. These differences could have arisen from the limitation of methods used in some of the studies including different age ranges for different studies and control for potentially confounding factors. In studies that have included women aged less than 60 years few women develop heart disease and, therefore, these studies were less powerful and could not identify an association. Studies that found positive associations included cases of all ages (see literature review, Tables 5-2, 5-3 and 5-4). Our study did not find a significant association between parity and reported CHD

events perhaps in part because of this age component. Not finding an association in our study does not mean that the association does not exist. The large cohort, case control and cross sectional studies showed small but consistent significant positive association between parity and CHD events among women. (Tables 5-2, 5-3 and 5-4 from the literature review).

14.3.2 Parity and the Metabolic Syndrome *(Hypothesis 8)*

The metabolic syndrome describes the co-occurrence of abnormalities in glucose and lipid metabolism, central fat distribution and blood pressure and indicates increased risk of future cardiovascular disease as well as diabetes. (For the definition of metabolic syndrome, see Appendix 2.) Whether parity plays a role in the development of the metabolic syndrome and therefore in CHD risk is a question not yet answered.

The metabolic syndrome was present in 58.3% of the women. Women with the metabolic syndrome had significantly higher parity and higher gravidity, p= 0.003 and p= 0.024 respectively. The association with live births was stronger than that with pregnancies. The women were significantly older and less likely to have secondary or higher education, were unemployed and more likely to be assisted by their daughters or daughters-in-law at home, and therefore more likely to be physically inactive. Women with the metabolic syndrome tended to have elevated DBP, SBP and hypertension and were menopausal. They tended to have higher rates of overall obesity, and central and abdominal obesity compared to those women without the metabolic syndrome. The metabolic syndrome was prevalent more among married and widowed women.

A significant association between parity in groups and the prevalence of the metabolic syndrome was observed, p=0.024. Adjustment for age slightly increased the magnitude of the association and it remained significant, p=0.038. Adjustment for educational level attenuated the association and it became non significant. Further adjustments for husband's educational level and marital status made no difference to the magnitude of the association and it remained non significant.

Our results based on models with parity as a continuous variable showed a 7% increase in the prevalence of the metabolic syndrome per extra child after adjustment

for age, women's and husband's education and marital status, marginally significant at p= 0.042. Further analysis suggested that physical inactivity as well as obesity (overall, central and abdominal obesity) play a vital role in the development of the metabolic syndrome on one hand and slightly mediate the association between parity and the development of the metabolic syndrome on the other. With such a marginal level of significance, and given the multiple testing involved in this study, the evidence for this association must be regarded with caution. However, the role of mediators is discussed.

The analysis was taken further, and details of the role of mediators and other correlates are shown in Table 13-4. In these regression models, all variables that were significantly associated with the metabolic syndrome were introduced into the model separately to test their roles individually and to determine if they act as mediators in the relationship between parity and the metabolic syndrome. Only those that showed a significant level were kept in the model.

None of the changes in the odds ratio for parity were very marked. Changes for physical activity and abdominal obesity were only from 1.07 to 1.06. For overall obesity, the change was from 1.07 to 1.05, suggesting small mediation from this source.

In summary, our study has shown as a cautious conclusion that the more children a woman has, the higher her risk of developing the metabolic syndrome. Women's sedentary lifestyle and lower education play a vital role in such an association by encouraging obesity and discouraging these women from seeking medical advice regarding their health. Most are unaware of the consequences of having elevated lipids, BP and weight increase, which can lead to metabolic syndrome and CHD risk.

This study shows the prevalence of the metabolic syndrome among Palestinian women living in the refugee camps for the first time, with a high prevalence of 58.3% using the IDF definition (recently approved by the WHO among others). This estimate is higher than that found by Al-Lawati et al among Omani adults where the prevalence of the metabolic syndrome was 21% using the ATP III definition [223]. Another study by Abdul-Rahim et al found that 17% of the West Bank rural and urban population had the metabolic syndrome using the WHO definition [232].

Different studies have used a variety of definitions for the metabolic syndrome including that of the WHO, the Adult Treatment Panel (ATP) III and the IDF which make comparison of findings more difficult and might explain the variation in results. Also the high rate of the metabolic syndrome could be linked to the high rate of central obesity (an important component of metabolic syndrome) among these women. However, none of these studies looked at parity as a risk factor for metabolic syndrome. This may be the first study that assesses the association between the prevalence of the metabolic syndrome and the number of live births in the Middle-East region, including Palestine.

There is little previous work with which to compare the present results. Only two recent studies, one in China and one in the US, have examined the association between parity and the metabolic syndrome, using the IDF definition and the ATP III definition respectively [164] [234]. The study carried out in China showed that higher parity was associated with a consistent increase in the risk of the metabolic syndrome among women and men after adjustment for age, socio-demographic, reproductive and behavioural factors. When the association was adjusted for BMI, it attenuated in men but not in women suggesting that the association with metabolic syndrome in women is likely to represent a biological response to pregnancy [164]. The study conducted in the US also found that the rate of the metabolic syndrome was significantly higher with increasing numbers of children, demonstrating a dose response relationship $P<0.0001$. The odds of having metabolic syndrome increased 13% with each additional child after controlling for age, race/ethnicity, income, and education, reproductive and behavioural risk factors. After adjustment for BMI, the strength of the association was decreased suggesting that weight might be an important mediator of the effect of parity on the risk of the metabolic syndrome [234].

Effective primary prevention requires an assessment of risk to categorize patients for selection of appropriate interventions. Therefore, in a separate analysis we have quantified the individual risk of developing CHD in 10 years time among these women by using the Framingham equation and then calculating the total risk factors score for each woman (see Appendix 2 for definition of the Framingham risk score). Our analysis has shown that 5.69% (26 women) were at higher risk of developing

CHD in 10 years time, 16.85% (77 women) were at medium risk, and 77.46% (345 women) at lower risk.

We also found that 10% of women with the MS are at higher risk of developing CHD in 10 years according to the Framingham score, while we found 28.9% of women with MS are at medium risk.

On an unadjusted basis we found that women's risk of developing CHD in 10 years increased by 0.003 per extra child, (95% CI: 0.002-0.005, $p<0.0001$). When adjusted for age the association became no more significant, but it must be remembered that age features in the Framingham score, so adjusting for it will tend to reduce these effects.

Identifying women at increased risk of developing MS and CHD will pave the way for primary prevention programmes that will target women and men at the same time and will save lives at the individual levels.

14.3.2.1 Study Limitations as related to the metabolic syndrome

Conclusions drawn from this cross-sectional design relating parity to the metabolic syndrome may be affected by several sources of bias as mentioned in the previous discussion sections:

Survival bias: Women with greater number of children might have an increased risk of premature death and also tend to have more of the metabolic syndrome; this would lead to underestimation of the strength of association between number of children and the metabolic syndrome. However, it seems unlikely that the association between the presence of the metabolic syndrome and parity was strongly affected by survival bias.

Participation bias: Participation bias is unlikely to account for the observed association between parity and metabolic syndrome. All women in the camps aged 40-65 years were recruited without knowing their number of children or whether or not they have the metabolic syndrome.

Reverse causality: It seems unlikely that metabolic syndrome leads to an increased number of children.

Recall bias: Women might not have been able to recall things that happened in the past such as their weight at age 18, and weight gain during each pregnancy. This has limited the use of such variables. Self-reporting of pregnancies could also be subject to recall bias. Live births are more likely to be fully recalled than number of pregnancies, since some pregnancy losses are clinically unrecognized and therefore not recalled [10]. Using parity minimizes this recall bias.

Although we have adjusted for confounders in the analysis, it would have been difficult to discount the role of unmeasured confounding factors in studying the association of parity with the metabolic syndrome. Socio-economic status may not have been adequately controlled by statistical adjustment for education. For example, we have used educational level as a proxy to socio-economic status; it was difficult to assess income so wealth status was used as a variable that created for the purpose of comparison among women. The same applies to physical activity and other behavioural risk factors.

Selection bias: The high response rate (all women recruited participated in the study except for 15 women who filled in the questionnaire but refused to give blood samples for reasons stated in the methods chapter) in the refugee camps means that selection bias is unlikely to be of concern.

14.3.2.2 Public Health Implications

The prevention and control of obesity plays a central role in the reduction in risk factors that make up the metabolic syndrome. The risk of developing abnormal glucose metabolism, dyslipidemia, and hypertension is markedly higher among people who are obese compared with people of normal weight [284]. Also, weight reduction through dietary and lifestyle modification and regular physical activity are shown to be effective in improving insulin sensitivity [285] [286], correcting metabolic abnormalities and reducing blood pressure in obese people [284]. Further research into those risk factors that can be modified, in particular obesity and physical inactivity, is highly recommended. Studies to examine the effect of lost pregnancies and breastfeeding on the development of the metabolic syndrome and its components would also be of interest.

The burden of CHD risk factors including prevention policies and programmes need to be addressed at the level of policy makers at the different ministries, WHO and UN organizations and NGOs. Prevention should always be the key strategy for avoiding the human and financial costs especially where resources are limited.

14.4. Conclusions

In the preceding sections of this chapter, we discussed some methodological limitations of this cross-sectional study as they emerged regarding parity and each of the risk factors for CHD, reported CHD and the metabolic syndrome. The following section assesses the strengths and weaknesses of the study as a whole. And, finally, it relates the study results to the original conceptual framework developed from the literature review

14.4.1 Overall Strengths of the Study

- The measurements for all outcome variables (lipids and lipoproteins, anthropometric outcomes, blood pressure, and diabetes) were determined by laboratory and physical measurements and not by self reporting.

- Standard quality control procedures were applied in the study at the level of the laboratory, equipment used and the data management analysis.

- The high commitment and dedication of the data collection team have added value to the study.

- The high participation rate of women in the study added value to the study. Women were very cooperative and participated willingly and cheerfully in spite of all the difficulties and the unstable environment they were living under. This was the first time in the lives of these women that someone was approaching them to study their health and well being.

- All authority bodies such as the Palestinian Ministry of Health, UNRWA, health professionals and health care providers, laboratory personnel, community leaders and women activists in the camps cooperated with the study.

- This study presents for the first time data on central and abdominal obesity at a time where data from the Arab region countries is scarce. Also this is the first study to present data on the prevalence of the metabolic syndrome in Palestinian refugee camps.

- For the study of parity, the great range of parity among the women has enhanced the power of the study

14.4.2 Overall Weaknesses of the Study

- Inclusion of men would have added value to the crucial issue of whether the observed association between the outcome variables including reported CHD, the metabolic syndrome and the 10-years CHD risk and parity was due to biological processes initiated by conception, or whether other mechanisms are involved including socio-demographic or lifestyle factors in response to pregnancy and/ or the raising of children. However, there are enough essential differences between men and women, both biological and behavioural, for this to be of only limited potential use.

- The women in this study are unlikely to completely represent older women among Palestinian refugees, on one hand, and older women among rural and urban areas of Palestine, on the other. Therefore inferring population prevalence from this study has to be dealt with cautiously.

- There might be unreliability in women's recall of CHD events and other reproductive health factors such as gravidity, pregnancy losses and other reproductive health variables and other covariates. CHD incidents were not measured clinically, as it was not part of the overall design of the study, but was added later as an additional analysis.

- Measurements of an exposure: there might be inaccuracy of women's recall. Pregnancy losses and thereby gravidity are less likely to be fully recalled compared to parity.

- The sample size, though evaluated at the planning stage, was not large in comparison with many other studies, giving less power, although the range of parity may have improved the power (see above).

- Some of the relationships such as parity and fasting blood sugar (FBS), and parity and decreased HDL-C levels were not detected in our study, although associations were found in other studies. This could be due to a lack of statistical power of this study given its smaller sample size.

- More sensitive instruments are needed to evaluate stress factors and levels (being an important risk factor for CHD) of this large group of women living in refugee camps and under constant stress. Imprecise measurement of stress may lead to inadequate control for it which in turn may lead to residual confounding. Retrospective studies with precise measure of stress factors are important to consider in future studies.

- Many hypotheses were investigated and even more statistical tests were carried out, leading to a greater chance of a significant result when the hypothesis was actually not true. There has been no specific adjustment for this, but we have drawn most attention to those findings that are supported by similar results from other studies, in the literature.

14.4.3 Recommendations for Future Studies

As the fertility rate falls, it would be of interest to assess whether the changes in reproductive patterns (decrease in fertility) have any effect on the development of the metabolic syndrome or any of its components in the near future, and whether this fall in fertility leads to a reduction in BMI, WC and W/H ratio among these women. The impact of parity seems to be more of less the same wherever you are, whether in the West or the Middle East or any part of the world.

A woman's education has an impact on limiting the number of children she will have. Being educated will offer women greater opportunity for employment which will in turn delay the age of marriage and reduce fertility.

It is not clear if the finding of the association between gravidity and FBS, which goes via failed pregnancies, is due to chance, or is a real association. This finding requires further investigation and is discussed further below.

14.4.4 Final summary and Relevance of the Study Results with the Conceptual Framework

An independent association was found between parity and BMI, on one hand, and parity and WC, on the other. These independent associations could not be explained by potential confounders and mediators, and are supported in other studies, and are more likely to represent a biological response to pregnancy. Changes in lifestyle accompanying raising children such as assistance in housework (a proxy to physical inactivity) partially mediated the association, but because it remained significant it seems to have an influence beyond these mediators. It is always possible that the association is due to unmeasured or residual confounders that we could not control for in our analysis. No evidence however was found of an association between parity and W/H ratio.

Among all of the lipids and lipoproteins, triglycerides (TG) showed a significant association with parity that was not explained by confounders. Increased TG levels in women with more children appeared to be partially mediated by overall obesity represented by BMI and sedentary lifestyle represented by assistance in housework. This suggests that the relationship between parity and triglycerides levels could be associated with the long term biological consequences of pregnancy through the alterations of lipid levels. The weight increase associated with pregnancy and/or the sedentary life style the women are leading partially transmits some of the effect of parity, but the association remained significant. On the other hand, no association between parity and decreased HDL-C was seen in our analysis. In view of evidence from other studies for this association, this could be due to lack of statistical power.

An association between parity and FBS did not emerge in our analysis and this also could be due to lack of statistical power. Among the confounders that were considered, the association seems to be explained most by age. Parity increased significantly with increasing age and the risk of diabetes increased significantly with

increasing age; age seemed to have a much stronger effect on the development of diabetes than parity.

In contrast, a significant association between gravidity and FBS was observed and could not be explained by confounders. This association was mediated mainly by failed pregnancies (the component of gravidity that also predicts FBS) and to a lesser extent by WC and WHR. It is not clear if this finding of the association between gravidity and FBS, which goes via failed pregnancies, is due to chance, or is a real association. Chance must be taken seriously because the result was not anticipated and because of the general caution over conducting many statistical tests. But the finding requires further investigation. Although parity is highly correlated with gravidity, these two factors are not interchangeable as the latter included abortions, miscarriages and still births and lacks breastfeeding. One would expect that the duration of childbearing and the intensity of the hormonal effects of pregnancy would be less than for a completed birth, and would therefore have weaker effects of pregnancies on FBS compared to that for live births, but this was not the case in this study. On the other hand, the whole hormonal profile of an incomplete pregnancy, with no subsequent breastfeeding, is basically different

Our results have also shown a positive crude association between number of children and elevated SBP. This association became non-significant after adjustment for age. No evidence of an association was observed between parity and DPB and hypertension in these older women. It might be that the power of the study was not sufficient to detect any significant association between parity and blood pressure among these older women. Thus, we must remain equivocal about the extent of a parity-hypertension association. The fact that there is a parity-obesity link, and also a link between obesity and hypertension might argue for such an association to exist in these women. The lack of direct evidence for it might be due to lack of power.

Only one outcome was not measured during the fieldwork, but was based on questionnaire responses. This was reported CHD events. No significant association was observed between parity in groups and these events after adjustment for age. Although CHD events were significantly associated with elevated SBP, hypertension and WHR, we could not detect a significant association and age seemed to exert a greater effect than parity on CHD events.

A significant age-adjusted association was observed between parity in groups and the development of the metabolic syndrome among these women. Women with a higher number of pregnancies and live births had a higher prevalence of the metabolic syndrome. Adjustment for educational level attenuated the association to the null hypothesis and it was no longer significant.

Clustering of the components of the metabolic syndrome increases the risk of CHD. There appears to be an association between parity and metabolic syndrome; there seems to be a biological side of the association that goes through pregnancy and childbirth, changing the lipid profile and carbohydrate metabolism, and over time this might lead to CHD events. This association seems to be confounded by the SES and in particular education and is mediated by the sedentary life style some women were leading. Central obesity which is a major component of the metabolic syndrome seems to exert a large effect, as a high percentage of women had central obesity. This could in part translate the higher rate of the metabolic syndrome among these women especially those with high parity. This implies again that efforts should be directed to the prevention and treatment of obesity in all its forms rather than to only address its associated co-morbidities.

From what has been stated so far, we can conclude that although older Palestinian women are different from Western women in bearing many children, being physically inactive, unemployed, with less educational attainment and not being smokers, the mechanism for the association between parity and CHD risk factors is likely to be the same. Parity exerts the same effect and the impact of parity would be the same whether among Palestinian women or among women from other countries or ethnic groups. Some differences might exist, for example, obesity and physical inactivity increasing with increasing number of children. Biologically, this would apply anywhere but in a western population obesity is not as directly linked to parity and women in Western countries do not commonly have their daughters or daughters-in-laws helping them in housework

The total fertility rate in Palestine has been reduced over recent years. The TFR dropped from 6.8 in 1992 to 4.6 in 2006 [287]. Will this decrease in TFR leads to a decrease in CHD events in women? Will it lead to a reduction of BMI and WC? Will

the lipid profile improve among women and therefore fewer CHD events will be observed? Does this fall in TFR have implications on CHD risk?

Among these Palestinian women, increased parity is significantly associated with obesity (as measured by BMI and waist circumference), triglycerides and an increased risk of the metabolic syndrome. Any of these, alone or in combination, could result in increased CHD risk for this group of women and a fall in average parity would then reduce these risks.

BIBLIOGRAPHY

1. World Health Organization, *Information sheet: facts related to chronic diseases and the WHO Global Strategy on Diet, Physical Activity and Health.* 2006.
2. Meilahn, E.N., R. Becker, and J. orrao, *Primary prevention of coronary heart disease in women.* Cardiology, 1995. **86**: p. 286-298.
3. LaRosa, J.C., *Women, lipoproteins and cardiovascular disease risk.* Can J Cardiol, 1990. **6 Suppl B**: p. 23B-29B.
4. Castelli, W.P., *Cardiovasculat disease in women.* Am J Obstet Gynecol, 1988. **158 (6Pt2)**: p. 1553-60, 1566-7.
5. Castanho, V.S., et al., *Sex differences in risk factors for coronary heart disease: a study in a Brazilian population.* BMC Public Health, 2001. **1**: p. 3.
6. Bjorkelund, C., et al., *Reproductive history in relation to relative weight and fat distribution.* Int J Obes Relat Metab Disord, 1996. **20**(3): p. 213-9.
7. Ness, R.B., et al., *Reproductive history and coronary heart disease risk in women.* Epidemiol Rev, 1994. **16**: p. 298-314.
8. Lawlor, D.A., et al., *Is the association between parity and coronary heart disease due to biological effects of pregnancy or adverse lifestyle risk factors associated with child-rearing? Findings from the British Women's Heart and Health Study and the British Regional Heart Study.* Circulation, 2003. **107**(9): p. 1260-4.
9. *Ministry of Health. Non Communicable Diseases. Health Status in Palestine 2005.* October 2006: p. 65.
10. Ministry, of, and Health, *Health Status in Palestine. The Annual Report 2004.* 2005.
11. United, N., *Report of the Commissioner general of the United Nations Relief and Works Agency for Palestine Refugees in the Near East.* 2005.
12. Abdul-Rahim, H.F., et al., *Obesity in a rural and an urban Palestinian West Bank population.* Int J Obes Relat Metab Disord, 2003. **27**(1): p. 140-6.
13. UNRWA, *Annual Report of the Department of Health.* 2007: p. 90-91.
14. Rizkallah, N., *Socio-economic and Health Profile of the Palestinian Arab Inhabitants of the Old City of Jerusalem.* 1996, Jerusalem-Vienna: Society for Austro-Arab Relations.
15. *Statistical Abstract of Israel.* 1995. **46**: p. 758.
16. UNICEF, *The State of the Palestinian Child in the West Bank and Gaza.* 1995: p. 4.
17. http://www.pcbs.gov.ps/Portals/_pcbs/PressRelease/worldpopday_e.pdf. [cited.
18. Ministry of Health (MOH), *The Status of the Health in Palestine, Annual report 2005, Palestine.* October 2006: p. 7.
19. Palestinian Central Bureau of Statistics, *Palestinian Family Health Survey, 2006: Final Report.* 2007.
20. Statistics, P.C.B.o., *Demographic and Health Survey.* 2004.
21. Ministry of Health (MOH), *The Status of the Health in Palestine, Annual report 2004, Palestine.* August 2005: p. I.
22. The World Bank, *West Bank and Gaza Update.* September 2006: p. 10.
23. The World Bank, *Poverty in the West bank and Gaza after Three Years of Economic Crisis.* November 2004: p. 11.
24. The Palestinian Central Bureau of Statistics, *The Population, Housing and Establishment Census - 2007, Press Conference on the Preliminary Findings, (Population, Buildings, Housing Units and Establishments), Ramallah, Palestine. February 2008.*
25. UNRWA's Website, *Available from: URL: http://www.un.org/unrwa/refugees/whois.html.*
26. UNRWA, *Annual Report of the Department of Health.* 2007: p. 18.
27. UNRWA, *Annual Report of the Department of Health.* 2005: p. I.
28. UNRWA, *Annual Report of the Department of Health.* 2007: p. 20.
29. Dr. Sandy Sufian, *Arab Health Care during the British Mandate, 1920-1947, in Separate and Cooperate, Cooperate and Separate: The Disengagement of the Palestine Health Care System from Israel and its Emergence as an Independent System.* 2002: p. 9-30.
30. Dr. Amin Khatib, *Eyewitness Account: Origins of the Palestinian Health System in the West Bank under Jordanian Rule and the Risa of the Non-Governmental Organizations.* 2002: p. 31-37.
31. *Check the website of the United Nations Relief and Works Agency for Palestine Refugees (UNRWA) www.un.org/unrwa.*

32. Abdul-Rahim, H., R. Giacaman, and L. Wick, *Health Sector Reform in the Occupied Palestinian Territories (OPT): Targeting the Forest or the Trees.* 2003: p. 6.
33. Barghouthi, M. and R. Giacaman, *The Emergence of an Infrastructure of Resistance: the Case of Health.* 1990: p. 2-3.
34. Barghouthi, M. and R. Giacaman, *The Emergence of an Infrastructure of resistance: the Case of Health in Nassar J and Heacock R eds. Intifada, OPT at the Crossroads* 1990, NY: Praeger. 73-87.
35. Za'noun Riad, *The long road to Independence in Health: A personal Account, in Separate and Cooperate, Cooperate and Separate: The Disengagement of the Palestine Health Care System from Israel and its Emergence as an Independent System* 2002: p. 136-147
36. Husseini, R., *The Introduction of Palestinian National Thinking Regarding Health Care, in Separate and Cooperate, Cooperate and Separate: The Disengagement of the Palestine Health Care System from Israel and its Emergence as an Independent System.* 2002: p. 154-176.
37. Ministry of Health (MOH), *The Status of Health in Palestine, Annual Report, Palestine, 2002, HMIS.* July 2003: p. 109.
38. HDIP, *Policy Dialogue Series, Coordination Workshops between the Health NGO Sector and the Palestinian Ministry of Health, 1996-2000.*
39. Ministry of Health (MOH), *The Status of the Health in Palestine, Annual Report, Paletine, 2002, HMIS.* 2003: p. 40.
40. Giacaman, R., H. Abdul-Rahim, and L. Wick, *Health Sector Reform in the Occupied Palestinian Territories (OPT): Tageting the Forest or the Trees?* . p. 7.
41. United Nations Unies, *The Humanitarian Impact of the West Bank Barrier on Palestinian Communities. Update No 4.* September 2004: p. 3.
42. Barghouti, M. and J. Jubran, *Health and Segragation: The Impact of the Israeli separation Wall on access to health care services, Health Development, Information and Policy Institute (HDIP).* 2005.
43. John Hopkins University and Al-Quds University, *Global Management Consulting Group and CARE International Nutritional Assessment and Sentinel Surveillance System for West Bank and Gaza.* August 2002: p. 3-16.
44. Ministry of Health (MOH), *The Status of the Health in Palestine, Annual report 2004, Palestine.* August 2005: p. 90.
45. Ministry of Health (MOH), *The Status of the Health in Palestine, Annual Report, Palestine, 2002, HMIS 2004.* July 2003: p. 309.
46. Palestinian Red Crescent Society (PRCS) and The Palestinian Medical Relief Society (PMRS) sources, September 2003.
47. in *Al-Ayam newspaper report.* 12 March 2001.
48. HSBR, *Yearly report May 2002-May 2003.* June 2003.
49. WHO, *Health Situation of Palestinian people living in the Occupied Palestinian Territory.* September 2002.
50. Palestine Monitor Website, www.palestinemonitor.org.
51. Director General of WHO Statement WHO/04, *"The Health situation in Palestine is deteriorating as a result of the escalation of the conflict, compounded by further border closure and curfews throughout the West bank and Gaza Strip since March 2002. There have been explicit restrictions on population movements, which hinder the delivery of health care services".* September 2002.
52. Medicins du Monde, *"Access to Health care and protection of the medical services in the Occupied and Autonomous Palestinian Territories".* November 2003.
53. The World Bank and UNESCO, *Donor Investment in Palestinian Development 1994-1998.* 1999: p. 26-27.
54. Ministry of Planning and International Cooperation and International Aid Coordination Department, *Monitoring Reports of Donors' Assistance.* June 2003: p. 1.
55. The World Bank Group, *One Year of Intifada. West Bank and Gaza Update, November.* 2001: p. 1.
56. The World Bank Group, *West Bank and Gaza Update, World Bank Report on the Impact of Intifada.* April-June 2003: p. 3-4.
57. Italian Cooperation Online Health Database, *http:healthprojects.itcoop-jer.org.*
58. Pfiefer Michaela, *Vulnerability and the International Health Response, an analysis of health and the health sector.* WHO and Peace Path Consulting, November 2001: p. 16.

59. OCHA, *Towards a More Secure Future: UN Agencies Operating in the Occupied Palestinian Territory Call for Action in Improving the Situation of Palestinian Women. Press release, International Women's Day, 8 March.* http://www.ochaopt.org. 2005.
60. Palestinian Centre for Human Rights, *The Integration of the Human Rights of Women and the Gender Perspective. Written Statement submitted to the 61st session of the UN Commission on Human Rights, 14 March-22 April.* http://domino.un.org/UNISPAL.NSF/0/bde61765flbec1de85256fbf005821ae? *Open Document.* 2005.
61. Ministry of Health (MOH), *The International Court of Justice: Israel Must Dismantle Wall, available from:* http://www.moh.gov.ps/index.asp?deptid=8&pranchid=61&action=details&serial=454. 2004.
62. Jubran Joan, *Health and Segregation II: The Impact of the Israeli Wall on access to Health care services, HDIP.* August 2005.
63. World Bank, *Gender Profile: West Bank and Gaza Strip, available from:* http://devdata.worldbank.org/genderstats/genderRpt.asp?rpt=profile&cty=WBG,West%20Bank%20and%20Gaza&hm=home. 2005.
64. Palestinian Medical relief Society, *Annual Report.* 2004.
65. Erturk, Y., *Integration of the Human Rights of Women and the Gender Perspective: Violence Against Women. Report of the Special Reporter on violence against women, its causes and consequences. UN Commission on Human Rights.* February 2005.
66. WHO, *Cardiovascular disease prevention and control available from:* http://www.who.int/dietphysicalactivity/publications/facts/cvd/en/index.html. 2003.
67. World Health Organization, *Cardiovascular Disease Prevention and Control available from:* www.who.int/mediacenter/factsheets/fs317/en/index.html. 2005.
68. Desmond, J. and C. Marley, *Coronary Heart Disease the facts.* 1991: Oxford University Press.
69. Pearson, T.A., D.T. Jamison, and J. Trejo-Gutierrez, *cardiovascular disease* in *Tamison DT. Disease control priorities in developing countries.* 1993, Oxford University Press for the World Bank.
70. Khaw, K.T. and S. Imogen, *Coronary Heart Disease in Women*, in *Coronary heart disease: are women special?*, I. Sharp, Editor. 1994, National Forum for Coronary Heart Disease Prevention.
71. Frank, B.H., M. Stampeer, and J. Manson, *Trends in the incidence of coronary heart disease and changes in diet and lifestyle in women.* The New England Journal of Medicine, 2000. **343**(8): p. 530-537.
72. Fletcher, A., *The epidemiology of cardiovascular disease in women.* Vascular Medicine Review, 1995. **6**: p. 17-31.
73. Sharp, I., *Attitudes to women and coronary heart disease*, in *Coronary heart disease:Are women special?*, I. Sharp, Editor. 1994, National Forum for Coronary Heart Disease Prevention.
74. Lawlor, D.A., et al., *Geographical variation in cardiovascular disease, risk factors, and their control in older women: British Women's Heart and Health Study.* J Epidemiol Community Health, 2003. **57**(2): p. 134-40.
75. Uemura, K. and Z. Pisa, *Trends in Cardiovascular Disease Mortality in Industrialized Countries Since 1950.* World Health Statistical Quarterely, 1988. **41**: p. 155-78.
76. Thom, T.J., *International Mortality from Heart Disease: Rates and Trends.* In J of Epidemiol, 1989. **18(supplement 1): S20-S28.**
77. McKeigue, P.M., *Rises and falls in coronary heart disease worldwide.* 1977.
78. WHO MONICA Project, *Monitoring Trends and Determinants in Cardiovascular Disease*, in *WHO Fact Sheet.* 1997
79. WHO Fact Sheet and *Preventing Chronic Diseases: a Vital Investment.* WHO Global report 2005 [cited.
80. Lawlor, D.A., S. Ebrahim, and G. Davey Smith, *A life course approach to coronary heart disease and stroke.* . Life course influences on Women's Health, ed. D. Kuh and R. Hardy. 2002, Oxford: Oxford University Press. 86-120.
81. Marmot, m.G. and E.J. Brunner, *CHD risk among women: Whitehall II and other studies*, in *Coronary heart disease: Are women special?*, I. Sharp, Editor. 1994, national Forum for Coronary Heart Disease: London. p. 57-70.

82. Kuller, L.H. and E.N. Meilahn, *Risk factors for cardiovascular disease among women.* Current Opinion in Lipidology, 1996. 7: p. 203-208.
83. Mikulec Katherine, Holloway Leah, and Krasnow Ruth, *Relationship of Endogenous Sex Hormones to Coronary Heart Disease: A Twin Study.* The Journal of Endocrinology and Metabolism, 2004. 89(3): p. 1240-1245.
84. Lawlor, D.A., S. Ebrahim, and S.C. Smith Jr, *Sex matters: secular and geographical trends in sex differences in coronary heart disease mortality.* BMJ, 2001. **323**: p. 541-545.
85. La Croix, A.X., J. Lang, and P. Scherr, *Smoking and mortality among older men and women in three communities.* N Engl J Med, 1991. **324**: p. 1619-25.
86. Jackson, G., *Coronary artery disease and women.* British medical Journal, 1994. **309**: p. 555-556.
87. Mann, J.I., M.P. Vessey, and M. Thorogood, *Myocardial infarction in young women with special reference to contraceptive practice.* Br Med J, 1975. **2**: p. 141-245.
88. Heiss, G., I. Tamir, and C.E. Davis, *Lipoprotein cholesterol distributions in selected North American populations: The Lipid Research Clinics Program Prevalence Study.* Circulation, 1988. **61**: p. 302-315.
89. Wood, D., *Lipid levels and coronary heart disease in women*, in *coronary heart disease: Are women special?*, I. Sharp, Editor. 1994, national Forum for Coronary Heart Disease Prevention.
90. Mann, J.I., B. Lewis, and J. Shepherd, *Blood lipid concentrations and other cardiovascular risk factors: distribution, prevalence and detection in Britian.* British Medical Journal, 1988. **296**: p. 1702-1706.
91. Stamler, J., P. Rhomberg, and J.A. Schoenberger, *Multivariate analysis for the relationship of seven variables to blood pressure. Findings of the Chicago Heart association detection project in industry, 1967-1972.* J Chron Dis, 1975. **28**: p. 527-48.
92. Higgins, M., J.B. Keller, and L.D. Ostrander, *Risk factors for coronary heart disease in women: Tecumseh Community Health Study, 1959-1980*, in *Coronary Heart Disease in Women*, E.D. Eaker, et al., Editors. 1987: New York: Haymarket Doyma. p. 83-89.
93. Bush, T.L., E. Barrett-Connor, and L.D. Cowan, *Cardiovascular mortality and noncontraceptive use of estrogen in women: results from the lipid research clinics program follow-up study.* Circulation, 1987. **75**: p. 1102-1109.
94. Barrett-Connor, E. and T.L. Bush, *Estrogen and coronary heart disease in women.* Jama, 1991. **265**(14): p. 1861-7.
95. Butler, W.J., et al., *Mortality from coronary heart disease in the Tecumseh Study.* Am J Epidemiol, 1985. **121**: p. 541-47.
96. Barrett-Connor, E., et al., *Sex differentials in Ischaemic Heart Disease Mortality in Diabetics.* Am J Epidemiol, 1983. **118**: p. 489-96.
97. Pan, W.H., L.B. Cedres, and K. Liu, *Relationship of clinical diabetes and asymptomatic hyperglycemia to risk of coronary disease mortality in men and women.* Am J Epidemiol, 1986. **123**: p. 504-16.
98. Lee, W., et al., *Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies.* Diabetes Care, 2000. **23**: p. 962-8.
99. Deborah Wexler, et al., *Sex Disparities in Treatment of Cardiac Risk Factors in Patients With Type 2 Diabetes.* Diabetes Care 2005. **28**(3): p. 514-520.
100. MacKeigue, P.M., B. Shah, and M.G. Marmot, *Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians.* Lancet, 1991. **337**: p. 382-386.
101. Lawlor, D.A., et al., *Sex differences in body fat distribution and carotid intima media thickness: cross sectional survey using data from the British regional heart study.* J Epidemiol Community Health, 2004. **58**(8): p. 700-4.
102. Manson, J.E., G. Colditz, and M.J. Stampfer, *A prospective study of obesity and risk of coronary heart doisease in women.* N Engl J Med, 1990. **322**: p. 882-89.
103. Bjorntorp, P., *The associations between obesity, adipose tissue distribution and disease.* Acta Med Scand, 1988. **723**: p. 121-134.
104. Lapidus, L., et al., *Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenburg, Sweden.* Br Med J (Clin Res Ed), 1984. **289**(6454): p. 1257-61.
105. Tremollieres, F., J. Pouilles, and C. Ribot, *Relative influence of age and menopause on total and regional body composition changes in postmenopausal women.* Am J Obstet Gynecol, 1996. **175**: p. 1594-600.

106. Larsson, B., et al., *Is abdominal body fat distribution a major explanation for the sex difference in the incidence of myocardial infarction? The study of men born in 1913 and the study of women, Goteborg, Sweden.* Am J Epidemiol, 1992. **135**(3): p. 266-73.
107. Lund, E., E. Arnesen, and J.K. Borgan, *Pattern of childbearing and mortality in married women--a national prospective study from Norway.* J Epidemiol Community Health, 1990. **44**(3): p. 237-40.
108. Beral, V., *Long term effects of childbearing on health.* J Epidemiol Community Health, 1985. **39**(4): p. 343-6.
109. Anand Sonia, et al., *Risk factors for Myocardial Infarction in Women and Men: Insight from the INTERHEART Study.* European Heart Journal, 2008. **29**: p. 932-940.
110. Ness, R.B., et al., *Number of pregnancies and the subsequent risk of cardiovascular disease.* N Engl J Med, 1993. **328**(21): p. 1528-33.
111. Green, A., V. Beral, and K. Moser, *Mortality in women in relation to their childbearing history.* Bmj, 1988. **297**(6645): p. 391-5.
112. Dekker, J.M. and E.G. Schouten, *Number of pregnancies and risk of cardiovascular disease.* N Engl J Med, 1993. **329**: p. 1893-1894.
113. Kvale, G., I. Heuch, and S. Nilssen, *Parity in relation to mortality and cancer incidence: a prospective study of Norwegian women.* Int J Epidemiol, 1994. **23**(4): p. 691-9.
114. Ness, R.B., et al., *Does number of children increase the rate of coronary heart disease in men?* Epidemiology, 1995. **6**(4): p. 442-5.
115. Steenland, K., C. Lally, and M. Thun, *Parity and coronary heart disease among women in the American Cancer Society CPS II population.* Epidemiology, 1996. **7**(6): p. 641-3.
116. Colditz, G.A., et al., *A prospective study of age at menarche, parity, age at first birth, and coronary heart disease in women.* Am J Epidemiol, 1987. **126**(5): p. 861-70.
117. Palmer, J.R., L. Rosenberg, and S. Shapiro, *Reproductive factors and risk of myocardial infarction.* Am J Epidemiol, 1992. **136**(4): p. 408-16.
118. Beard, C.M., V. Fuster, and J.F. Annegers, *Reproductive history in women with coronary heart disease. A case-control study.* Am J Epidemiol, 1984. **120**(1): p. 108-14.
119. Winkelstein, W., Jr. and A.C. Rekate, *Age Trend of Mortality from Coronary Artery Disease in Women and Observations on the Reproductive Patterns of Those Affected.* Am Heart J, 1964. **67**: p. 481-8.
120. Winkelstein, W., Jr., M.A. Stenchever, and A.M. Lilienfeld, *Occurrence of pregnancy, abortion, and artificial menopause among women with coronary artery disease: a preliminary study.* J Chronic Dis, 1958. **7**(4): p. 273-86.
121. Mant, D., et al., *Myocardial infarction and angina pectoris in young women.* J Epidemiol Community Health, 1987. **41**(3): p. 215-9.
122. Talbott, E.O., et al., *Reproductive history of women dying of sudden cardiac death: a case-control study.* Int J Epidemiol, 1989. **18**(3): p. 589-94.
123. Croft, P. and P.C. Hannaford, *Risk factors for acute myocardial infarction in women: evidence from the Royal College of General Practitioners' oral contraception study.* Bmj, 1989. **298**(6667): p. 165-8.
124. La Vecchia, C., et al., *Menstrual and reproductive factors and the risk of myocardial infarction in women under fifty-five years of age.* Am J Obstet Gynecol, 1987. **157**(5): p. 1108-12.
125. Oliver, M.F., *Ischaemic heart disease in young women.* Br Med J, 1974. **4**(5939): p. 253-9.
126. Mann, J.I. and W.H. Inman, *Oral contraceptives and death from myocardial infarction.* Br Med J, 1975. **2**(5965): p. 245-8.
127. Mann, J.I., et al., *Myocardial infarction in young women with special reference to oral contraceptive practice.* Br Med J, 1975. **2**(5965): p. 241-5.
128. Rosenberg L, Miller DR, and Kaufman DW, *Myocardial infarction in women under 50 years of age.* JAMA, 1983. **250**: p. 2801-6.
129. Wolff, B., et al., *Relation of parity with common carotid intima-media thickness among women of the Study of Health in Pomerania.* Stroke, 2005. **36**(5): p. 938-43.
130. Humphries, K.H., et al., *Parity and carotid artery atherosclerosis in elderly women: The Rotterdam Study.* Stroke, 2001. **32**(10): p. 2259-64.
131. Hardy, R., et al., *Number of children and coronary heart disease risk factors in men and women from a British birth cohort.* International Journal of Obstetrics and Gynaecology, 2007. **114**: p. 721-730.
132. Bray JH and Hetherington EM, *Families in transition: introduction and overview.* J Fam Psychol, 1993. **7**: p. 3-8.

133. Croft, P. and P. Hannaford, *Risk factors for acute myocardial infarction in women.* Bmj, 1989. **298**(6674): p. 674.
134. Kaye, S.A., et al., *The association of body fat distribution with lifestyle and reproductive factors in a population study of postmenopausal women.* Int J Obes, 1990. **14**(7): p. 583-91.
135. Rodin, J., et al., *Weight cycling and fat distribution.* Int J Obes, 1990. **14**(4): p. 303-10.
136. den Tonkelaar, I., et al., *Fat distribution in relation to age, degree of obesity, smoking habits, parity and estrogen use: a cross-sectional study in 11,825 Dutch women participating in the DOM-project.* Int J Obes, 1990. **14**(9): p. 753-61.
137. Blaudeau, T.E., G.R. Hunter, and B. Sirikul, *Intra-abdominal adipose tissue deposition and parity.* Int J Obes (Lond), 2006. **30**(7): p. 1119-24.
138. Linne, Y., et al., *Weight development over time in parous women--the SPAWN study--15 years follow-up.* Int J Obes Relat Metab Disord, 2003. **27**(12): p. 1516-22.
139. Kritz-Silverstein, D., E. Barrett-Connor, and D.L. Wingard, *The effect of parity on the later development of non-insulin-dependent diabetes mellitus or impaired glucose tolerance.* N Engl J Med, 1989. **321**(18): p. 1214-9.
140. Kritz-Silverstein, D., E. Barrett-Connor, and D.L. Wingard, *The relationship between multiparity and lipoprotein levels in older women.* J Clin Epidemiol, 1992. **45**(7): p. 761-7.
141. Lewis, C.E., et al., *Adverse effect of pregnancy on high density lipoprotein (HDL) cholesterol in young adult women. The CARDIA Study. Coronary Artery Risk Development in Young Adults.* Am J Epidemiol, 1996. **144**(3): p. 247-54.
142. Gunderson, E.P., et al., *Long-term plasma lipid changes associated with a first birth. The CARDIA study.* Am J Epidemiol, 2004. **159**: p. 1028-1039.
143. Weng, H.H., et al., *Number of children associated with obesity in middle-aged women and men: results from the health and retirement study.* J Womens Health (Larchmt), 2004. **13**(1): p. 85-91.
144. Kim, S.A., A.D. Stein, and R. Martorell, *Country development and the association between parity and overweight.* Int J Obes (Lond), 2006.
145. Martorell, R., *Obesity in the Developing World*, in *The Nutrition Transition: Diet and Disease in the Developing World.* Caballero B and Popkin BM, Editors. 2002, Academic Press: Boston. p. 147-164.
146. Murphy, J.F., *The National Taskforce on Obesity.* Ir Med J, 2005. **98**(5): p. 132.
147. Kopelman, P.G., *Obesity as a medical problem.* Nature, 2000. **404**(6778): p. 635-43.
148. Must, A., et al., *The disease burden associated with overweight and obesity.* Jama, 1999. **282**(16): p. 1523-9.
149. Krauss, R.M., et al., *Obesity : impact on cardiovascular disease.* Circulation, 1998. **98**(14): p. 1472-6.
150. Soler J. T, et al., *Association of body fat distribution with plasma lipids, lipoproteins, apolipoproteins AI and B in postmenopausal women.* J Clin Epidemiol, 1988. **41**(11): p. 1075-81.
151. Campaigne, B.N., *Body fat distribution in females: metabolic consequences and implications for weight loss.* Med Sci Sports Exerc, 1990. **22**(3): p. 291-7.
152. Siega-Riz, A.M., K.R. Evenson, and N. Dole, *Pregnancy-related weight gain--a link to obesity?* Nutr Rev, 2004. **62**(7 Pt 2): p. S105-11.
153. Heliovaara, M. and A. Aromaa, *Parity and obesity.* J Epidemiol Community Health, 1981. **35**(3): p. 197-9.
154. Weinsier, R.L., et al., *Body fat distribution in white and black women: different patterns of intraabdominal and subcutaneous abdominal adipose tissue utilization with weight loss.* Am J Clin Nutr, 2001. **74**: p. 631-6.
155. Terry, R., W. Page, and W. Haskell, *Waist/hip ratio, body mass index and premature cardiovascular disease mortality in US Army veterans duringa twenty-three year follow-up study.* International Journal of Obesity, 1992. **16**: p. 417-423.
156. Sadurskis, A., et al., *Energy metabolism, body composition, and milk production in healthy Swedish women during lactation.* Am J Clin Nutr, 1988. **48**(1): p. 44-9.
157. Forster, J.L., et al., *Reproductive history and body mass index in black and white women.* Prev Med, 1986. **15**(6): p. 685-91.
158. Brown, J.E., S.A. Kaye, and A.R. Folsom, *Parity-related weight change in women.* Int J Obes Relat Metab Disord, 1992. **16**(9): p. 627-31.
159. Parham, E.S., M.F. Astrom, and S.H. King, *The association of pregnancy weight gain with the mother's postpartum weight.* J Am Diet Assoc, 1990. **90**(4): p. 550-4.

160. Noppa, H. and C. Bengtsson, *Obesity in relation to socioeconomic status. A population study of women in Goteborg, Sweden.* J Epidemiol Community Health, 1980. **34**(2): p. 139-42.
161. Tonkelaar, I.D., et al., *Factors influencing waist/hip ratio in randomly selected pre- and post-menopausal women in the dom-project (preliminary results).* Int J Obes, 1989. **13**(6): p. 817-24.
162. Rissanen, A.M., et al., *Determinants of weight gain and overweight in adult Finns.* Eur J Clin Nutr, 1991. **45**(9): p. 419-30.
163. Gunderson, E.P., et al., *Development of overweight associated with childbearing depends on smoking habit: The Coronary Artery Risk Development in Young Adults (CARDIA) Study.* Obes Res, 2004. **12**(12): p. 2041-53.
164. Coitinho, D.C., R. Sichieri, and M.H. D'Aquino Benicio, *Obesity and weight change related to parity and breast-feeding among parous women in Brazil.* Public Health Nutr, 2001. **4**(4): p. 865-70.
165. Rooney, B.L. and C.W. Schauberger, *Excess pregnancy weight gain and long-term obesity: one decade later.* Obstet Gynecol, 2002. **100**(2): p. 245-52.
166. Brewer, M.M., M.R. Bates, and L.P. Vannoy, *Postpartum changes in maternal weight and body fat depots in lactating vs nonlactating women.* Am J Clin Nutr, 1989. **49**(2): p. 259-65.
167. Rebuffe-Scrive, M., et al., *Fat cell metabolism in different regions in women. Effect of menstrual cycle, pregnancy, and lactation.* J Clin Invest, 1985. **75**(6): p. 1973-6.
168. Manning-Dalton, C. and L. Allen, *The effects of lactation on energy and protein consumption, postpartum weight change and body composition of well nourished North American women.* Nutr Res, 1983. **3**: p. 293-308.
169. Quandt, S.A., *Changes in maternal postpartum adiposity and infant feeding patterns.* Am J Phys Anthropol, 1983. **60**: p. 455-61.
170. Kac, G., et al., *Gestational weight gain and prepregnancy weight influence postpartum weight retention in a cohort of brazilian women.* J Nutr, 2004. **134**(3): p. 661-6.
171. Bastian, L.A., et al., *Number of children and the risk of obesity in older women.* Prev Med, 2005. **40**(1): p. 99-104.
172. Frisch, R.E. and J.W. McArthur, *Menstrual cycles: fatness as a determinant of minimum weight for height necessary for their maintenance or onset.* Science, 1974. **185**(4155): p. 949-51.
173. Lindquist, O. and C. Bengtsson, *Serum lipids, arterial blood pressure and body weight in relation to the menopause: results from a population study of women in Goteborg, Sweden.* Scand J Clin Lab Invest, 1980. **40**(7): p. 629-36.
174. Saadi, H.F., et al., *Hypothesis: Correction of low vitamin D status among Arab women will prevent heart failure and improve cardiac function in established heart failure.* Eur J Heart Fail, 2006. **8**(7): p. 694-6.
175. Bernstein, L., et al., *Estrogen and sex hormone-binding globulin levels in nulliparous and parous women.* J Natl Cancer Inst, 1985. **74**(4): p. 741-5.
176. Harris, H.E., et al., *Are overweight women at increased risk of obesity following pregnancy?* Br J Nutr, 1998. **79**(6): p. 489-94.
177. Newcombe, R.G., *Development of obesity in parous women.* J Epidemiol Community Health, 1982. **36**(4): p. 306-9.
178. Lahmann, P.H., et al., *Sociodemographic factors associated with long-term weight gain, current body fatness and central adiposity in Swedish women.* Int J Obes Relat Metab Disord, 2000. **24**(6): p. 685-94.
179. Kritz, S., E. Barrett-Connor, and N.J. Friedlander, *Parenthood and lipid and lipoprotein levels in older men.* Ann Epidemiol, 1997. **7**(4): p. 275-9.
180. Barrett-Connor, E., *Sex differences in coronary heart disease. Why are women so superior? The 1995 Ancel Keys Lecture.* Circulation, 1997. **95**(1): p. 252-64.
181. Lao, X.Q., et al., *Parity and the metabolic syndrome in older Chinese women: the Guangzhou Biobank Cohort Study.* Clin Endocrinol (Oxf), 2006. **65**(4): p. 460-9.
182. Grinblatt, J.A., *Number of pregnancies and risk of cardiovascular disease.* N Engl J Med, 1993. **329**(25): p. 1893; author reply 1894-5.
183. Wardle, J., J. Waller, and M.J. Jarvis, *Sex differences in the association of socioeconomic status with obesity.* Am J Public Health, 2002. **92**(8): p. 1299-304.
184. Gunderson, E.P., et al., *Excess gains in weight and waist circumference associated with childbearing: The Coronary Artery Risk Development in Young Adults Study (CARDIA).* Int J Obes Relat Metab Disord, 2004. **28**(4): p. 525-35.

185. Smith, D.E., et al., *Longitudinal changes in adiposity associated with pregnancy. The CARDIA Study. Coronary Artery Risk Development in Young Adults Study.* Jama, 1994. **271**(22): p. 1747-51.
186. Sohlstrom, A. and E. Forsum, *Changes in adipose tissue volume and distribution during reproduction in Swedish women as assessed by magnetic resonance imaging.* Am J Clin Nutr, 1995. **61**: p. 287-295.
187. Hunter, G.R., et al., *Intra-abdominal adipose tissue values associated with risk of possessing elevated blood lipids and blood pressure.* Obes Res, 1994. 2(6): p. 563-8.
188. Smith, D.E., et al., *Longitudinal changes in adiposity associated with pregnancy. The CARDIA study. Coronary artery risk development in young adults.* JAMA, 1994. **271**: p. 1747-1751.
189. Noppa, H., et al., *Obesity in relation to morbidity and mortality from cardiovascular disease.* Am J Epidemiol, 1980. **111**(6): p. 682-92.
190. Potter, J.M. and P.J. Nestel, *The hyperlipidemia of pregnancy in normal and complicated pregnancies.* Am J Obstet Gynecol, 1979. **133**(2): p. 165-70.
191. Knopp, R.H., et al., *Effects of pregnancy, postpartum lactation, and oral contraceptive use on the lipoprotein cholesterol/triglyceride ratio.* Metabolism, 1985. **34**(10): p. 893-9.
192. Miller, V.T., *Dyslipoproteinemia in women. Special considerations.* Endocrinol Metab Clin North Am, 1990. **19**(2): p. 381-98.
193. van Stiphout, W.A., A. Hofman, and A.M. de Bruijn, *Serum lipids in young women before, during, and after pregnancy.* Am J Epidemiol, 1987. **126**(5): p. 922-8.
194. Knopp, R.H., et al., *Population-based lipoprotein lipid reference values for pregnant women compared to nonpregnant women classified by sex hormone usage.* Am J Obstet Gynecol, 1982. **143**(6): p. 626-37.
195. Qureshi, I.A., et al., *Hyperlipidaemia during normal pregnancy, parturition and lactation.* Ann Acad Med Singapore, 1999. **28**(2): p. 217-21.
196. Bush, T.L., L.P. Fried, and E. Barrett-Connor, *Cholesterol, lipoproteins, and coronary heart disease in women.* Clin Chem, 1988. **34**(8B): p. B60-70.
197. Bush, T.L., *The epidemiology of cardiovascular disease in postmenopausal women.* Ann N Y Acad Sci, 1990. **592**: p. 263-71; discussion 334-45.
198. LaRosa, J., *Lipids and cardiovascular disease: do the findings and therapy apply equally to men and women?* Womens Health issues, 1992. 2(2): p. 102-11; discussion 111-3.
199. Sirikulchayanonta, C., W. Singsurapap, and W. Phuapradit, *The effect of parity on lipid profile in normal pregnant women.* J Med Assoc Thai, 2000. **83 Suppl 1**: p. S141-5.
200. Hubert, H.B., et al., *Life-style correlates of risk factor change in young adults: an eight-year study of coronary heart disease risk factors in the Framingham offspring.* Am J Epidemiol, 1987. **125**(5): p. 812-31.
201. Flegal KM, Ness RB, and Kramer RA, *Parity and High Density Lipoprotein Cholesterol Levels in White Women from the Second National Health and Nutrition Examination Survey (NHANES II). Abstract).* Am J Epidemiol, 1990. **132**: p. 766.
202. Haertel V, Heiss G, and Filipiak B, *Cross-sectional and longitudinal associations between high density lipoprotein cholesterol and women's employment.* Am J Epidemiol, 1992. **135**: p. 68-78.
203. Nicholson, W.K., et al., *Parity and risk of type 2 diabetes: the Atherosclerosis Risk in Communities Study.* Diabetes Care, 2006. **29**(11): p. 2349-54.
204. Hanley, A.J., et al., *Association of parity with risk of type 2 diabetes and related metabolic disorders.* Diabetes Care, 2002. **25**(4): p. 690-5.
205. Kuhl, C., *Glucose metabolism during and after pregnancy in normal and gestational diabetic women. Influence of normal pregnancy on serum glucose and insulin concentartion during basal fasting conditions and after a challenge with glucose.* Acta Endocrinol, 1975. **79**: p. 709-19.
206. Bleicher, S.J., J.B. O'Sullivan, and N. Freinkel, *Carbohydrate Metabolism in Pregnancy. V. the Interrelations of Glucose, Insulin and Free Fatty Acids in Late Pregnancy and Post Partum.* N Engl J Med, 1964. **271**: p. 866-72.
207. O'Sullivan, J.B., *Body weight and subsequent diabetes mellitus.* Jama, 1982. **248**(8): p. 949-52.
208. Freinkel, N., *Banting Lecture 1980. Of pregnancy and progeny.* Diabetes, 1980. **29**(12): p. 1023-35.
209. Pyke, D.A., *Parity and the incidence of diabetes.* Lancet, 1956. **270**: p. 818-2.

210. Fitzgerald, M.G., et al., *The effect of sex and parity on the incidence of diabetes mellitus.* Q J Med, 1961. **30**: p. 57-70.
211. Manson, J.E., et al., *Parity and incidence of non-insulin-dependent diabetes mellitus.* Am J Med, 1992. **93**(1): p. 13-8.
212. Alderman, B.W., et al., *Reproductive history, glucose tolerance, and NIDDM in Hispanic and non-Hispanic white women. The San Luis Valley Diabetes Study.* Diabetes Care, 1993. **16**(12): p. 1557-64.
213. Collins, V.R., G.K. Dowse, and P.Z. Zimmet, *Evidence against association between parity and NIDDM from five population groups.* Diabetes Care, 1991. **14**(11): p. 975-81.
214. Boyko, E.J., et al., *Effects of childbearing on glucose tolerance and NIDDM prevalence.* Diabetes Care, 1990. **13**(8): p. 848-54.
215. Simmons, D., *Parity, ethnic group and the prevalence of type 2 diabetes: the Coventry Diabetes Study.* Diabet Med, 1992. **9**(8): p. 706-9.
216. Cheung, N.W., *Is parity associated with earlier diagnosis of type 2 diabetes?* Diabetes Res Clin Pract, 2004. **66**(3): p. 287-91.
217. Bener, A., M. Zirie, and A. Al-Rikabi, *Genetics, obesity, and environmental risk factors associated with type 2 diabetes.* Croat Med J, 2005. **46**(2): p. 302-7.
218. Kritz-Silverstein, D., D.L. Wingard, and E. Barrett-Connor, *The relation of reproductive history and parenthood to subsequent hypertension.* Am J Epidemiol, 1989. **130**(2): p. 399-403.
219. Lee-Feldstein, A., E. Harburg, and E. Hauenstein, *Parity and blood pressure among four race-stress groups of females in Detroit.* Am J Epidemiol, 1980. **111**: p. 356-366.
220. RaO, P.S., S.G. Inbaraj, and S. V.R., *Blood pressure measures among women in South India.* J Epidemiol Community Health, 1984. **38**: p. 49-53.
221. Barnes, J. and F.J. Browne, *Blood pressure and the incidence of hypertension in nulliparous and parous women in relation to the remote prognosis of the toxemias of pregnancy.* J Obstet Gynaecol Br Emp, 1945. **52**: p. 1-12.
222. Johnson, B.C. and R.D. Remington, *A sampling study of blood pressure levels in White and Negro residents of Nassau, Bahamas.* J Chronic Dis, 1961. **13**: p. 39-51.
223. Parry, E.H.O., *Ethiopian cardiovascular studies. III. The causal blood pressure in Ethiopian high-landers in Addis Ababa.* East Afr Med J, 1969. **46**: p. 246-56.
224. Akinkugbe, A., *Arterial pressures in nonpregnant women of childbearing age in Ile-Ife, Nigeria.* Br J Obstet Gynaecol, 1976. **83**: p. 545-9.
225. Humerfelt, S. and F. Wedervang, *A study of the influence upon blood pressure of marital status, number of children and occupation.* Acta Med Scand 1957. **159**: p. 489-97.
226. Miall, W.E. and P.D. Oldham, *Factors influencing arterial blood pressure in the general population.* Clin Sci, 1958. **17**: p. 409-44.
227. Miall, W.E. and P.D. Oldham, *Follow-up study of arterial pressure in the population of Welsh Mining Valley.* Br Med J, 1959. **2**: p. 1204-1210.
228. Ree, G.H., *Arterial pressures in a West African (Gambian) rural population.* J Trop Med Hyg, 1973. **76**: p. 65-70.
229. Strevens, H., D. Wide-Swensson, and I. Ingemarsson, *Blood pressure during pregnancy in a Swedish population; impact of parity.* Acta Obstet Gynecol Scand, 2001. **80**(9): p. 824-9.
230. Duda, R.B., et al., *Results of the Women's Health Study of Accra: Assessment of blood pressure in urban women.* Int J Cardiol, 2006.
231. Miall, W.E., E.H. Kass, and J. Ling, *factors influencing arterial blood pressure in the general population in Jamaica.* Br Med J, 1962. **2**: p. 497-506.
232. Ness, R.B., R.A. Kramer, and K.M. Flegal, *Gravidity, blood pressure, and hypertension among white women in the Second National Health and Nutrition Examination Survey.* Epidemiology, 1993. **4**(4): p. 303-9.
233. Schneckloth, R.E., A.C. Corcoran, and K.L. Stuart, *Arterial pressure and hypertensive disease in a West Indian Negro population. Report of a survey in St. Kitts, West Indies.* Am Heart J, 1962. **63**: p. 607-628.
234. Johnson, B.C. and R.D. Remington, *A sampling study of blood pressure levels in White and Nigro residents of Nassau, Bahamas.* J Chronic Dis, 1961. **13**: p. 39-51.
235. *Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report.* Circulation, 2002. **106**(25): p. 3143-421.

236. Ninomiya, J.K., et al., *Association of the metabolic syndrome with history of myocardial infarction and stroke in the Third National Health and Nutrition Examination Survey.* Circulation, 2004. **109**(1): p. 42-6.
237. Lakka, H.M., et al., *The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men.* Jama, 2002. **288**(21): p. 2709-16.
238. Isomaa, B., et al., *Cardiovascular morbidity and mortality associated with the metabolic syndrome.* Diabetes Care, 2001. **24**(4): p. 683-9.
239. Lorenzo, C., et al., *The metabolic syndrome as predictor of type 2 diabetes: the San Antonio heart study.* Diabetes Care, 2003. **26**(11): p. 3153-9.
240. Al-Lawati, J.A., et al., *Prevalence of the metabolic syndrome among Omani adults.* Diabetes Care, 2003. **26**(6): p. 1781-5.
241. Al-Lawati, J.A., et al., *Increasing prevalence of diabetes mellitus in Oman.* Diabet Med, 2002. **19**(11): p. 954-7.
242. Al-Mahroos, F. and P.M. McKeigue, *High prevalence of diabetes in Bahrainis. Associations with ethnicity and raised plasma cholesterol.* Diabetes Care, 1998. **21**(6): p. 936-42.
243. Abdalla, N., et al., *Non-insulin dependent diabetes in Kuweit: prevalence rates and associated risk factors.* Diabetes Res Clin Pract, 1998. **42**: p. 187-196.
244. Jaddou, H.Y., A.M. Batiehah, and K.M. Ajlouni, *Prevalence and associated factors of hypertension: results from a three community-based survey, Jordan.* J Hum Hypertens, 1996. **10**(12): p. 815-21.
245. El Mugamer, I.T., et al., *Diabetes, obesity and hypertension in urban and rural people of bedouin origin in the United Arab Emirates.* J Trop Med Hyg, 1995. **98**: p. 407-415.
246. Al-Nuaim, A.R., *Prevalence of glucose intolerance in urban and rural communities in Saudi Arabia.* Diabet Med, 1997. **14**(7): p. 595-602.
247. al-Isa, A.N., *Prevalence of obesity among adult Kuwaitis: a cross-sectional study.* Int J Obes Relat Metab Disord, 1995. **19**(6): p. 431-3.
248. Hassab, A.A., A. Jaffar, and Z. Hallaj, *Blood pressure patterns among the Omani population.* East Mediterr Health J 1999. **5**: p. 46-54.
249. Abdul-Rahim, H.F., et al., *The metabolic syndrome in the West Bank population: an urban-rural comparison.* Diabetes Care, 2001. **24**(2): p. 275-9.
250. World Health Organization, *Definition, Diagnosis and Classification of Diabetes mellitus and its Complications. Part I: Diagnosis and Classification of Diabetes Mellitus.* (WHO/NCD/NCS/99.2). 1999, Geneva: WHO.
251. Cohen, A., et al., *Number of children and risk of metabolic syndrome in women.* J Womens Health (Larchmt), 2006. **15**(6): p. 763-73.
252. Alberti, K.G., P. Zimmet, and J. Shaw, *Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation.* Diabet Med, 2006. **23**(5): p. 469-80.
253. Rossner, S., *Pregnancy, weight cycling and weight gain in obesity.* Int J Obes Relat Metab Disord, 1992. **16**(2): p. 145-7.
254. Lissner, L., P.M. Odell, and R.B. D'Agostino, *Variability of body weight and health outcomes in the Framingham population.* N Engl J Med, 1991. **324**: p. 1839-44.
255. Karasek, R., D. Baker, and F. Marxer, *Job description latitude, job demands and cardiovascular disease: a prospective study of swedish men.* Am J Public Health, 1981. **71**: p. 694-705.
256. La Rosa, J.C., *the varying effects of progestins on lipid levels and vcardiovascular disease.* Am J Obstet Gynecol, 1988. **158**: p. 1621-9.
257. UNRWA. *Refugee Camp Profile: West Bank Field Office, www.un.org/unrwa/refugees/westbank/amari.html*. [cited.
258. UNRWA. *Refugee Camps Profile: West Bank Field Office, www.un.org/unrwa/refugees/westbank/kalandia.html*. [cited.
259. Grodon, T., C.W. P., and H.M. C., *High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study.* Am J Med, 1977. **62**: p. 707-714.
260. Brunner, D., J. Weisbort, and N. Meshulam, *Relation of serum total cholesterol and high-density lipoprotein cholesterol percentage to the incidence of definite coronary events: twenty-year follow-up of Donolo Tel-Aviv prospective coronary artery disease study.* Am J Cardiol, 1987. **59**: p. 1271-1276.
261. Manolio, T.A., T. Pearson, and N.K. Wenger, *Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop.* Ann Epidemiol, 1992. **2**: p. 161-176.

262. Lerner, D.J. and W.B. Kannel, *Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-upof the Framingham population.* Am Heart J, 1986. **111**: p. 383-90.
263. Gordon, D.J., J.L. Probstfield, and R.J. garrison, *High density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies.* Circulation, 1989. 79: p. 8-15.
264. Heiss, G., N.J. Johnson, and S. Reiland, *The epidemiology of plasma high-density lipoprotein cholesterol levels. The Lipid Research Clinics Program Prevalence Study.* Circulation, 1980. **62 (Suppl.IV)**: p. 116-135.
265. World Health Organization, *Physical status: the use and interpretation of anthropometry. Report of WHO expert committee.* Technical Report Series No 854. 1995, Geneva: WHO.
266. World Health Organization, *International Task Force for the Prevention of CHD available from http://www.chd-taskforce.com/.*
267. *Diabetes Mellitus: Report of a WHO Study Group. World Health Organization Technical report Series.* 1980. **646**: p. 1-80.
268. *Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus.* Diabetes Care, 1997. **20**(1183-97).
269. *The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood pressure. US Department of Health and Human Services. National Institutes of Health, National Heart, Lung and Blood Institute* 2004.
270. Olinto, M.T.A., et al., *Waist circumference as a determinant of hypertension and diabetes in Brazilian women: a population-based study.* Public Health Nutr, 2003. 7(5): p. 629-635.
271. Chumlea WC, Baumgartner RN, and Garry PJ, *Fat distribution and blood lipids in a sample of healthy elderly poeple.* Int J obesity, 1992. **16**: p. 125-133.
272. UNRWA, *United Nations Relief and Works Agency for Palestine Refugees in the Near East. Annual Reort of the Department of Health.* 1995.
273. Fidanza, F., *Anthropometric methodology. In: Nutritional Status Assessment. A manual for Population Studies*, ed. F. Fidanza. 1991: Chapman and Hall. 1-44.
274. Khattab, H., *The Silent Endurance: Social Conditions of Women's Reproductive Health in Rural Egypt.* 1992: Unicef and Population Council.
275. Erem, C., et al., *Prevalence of obesity and associated risk factors in a Turkish population (trabzon city, Turkey).* Obes Res, 2004. **12**(7): p. 1117-27.
276. Jia, W.P., K.S. Xiang, and L. Chen, *Epidemiological study on obesity and its comorbidities in urban Chinese older than 20 years of age in Shanghai, China.* Obes Rev, 2002. **3**: p. 157-65.
277. Kark, J.D., S. Goldman, and L. Epstein, *Iraqi missile attacks on Israel. The association of mortality with a life-threatening stressor.* JAMA, 1995. **273**: p. 1208-1210.
278. Zwi, A. and A. Ulgate, *Towards an epidemiology of political violence in the Third World.* Soc Sci Med, 1989. **28**: p. 633-642.
279. Meisel, S.R., et al., *Effect of Iraqi missile war on incidence of acute mayocardial infarction and sudden death in Israeli civilians.* Lancet, 1991. **ii**: p. 660-661.
280. Slater, P.E., *The Gulf war and mortality in Isreal.* Lancet, 1991. **ii**: p. 1336 (letter).
281. Osman, M., H. Rashad, and F. Roudi-Fahimi. *Population Reference Bureau, Marriage In The Arab World, http://www.prb.org/pdf05/MarriageInArabWorld_Eng.pdf, retrieved July 2008.* [cited.
282. Jabbour, S. *Health and Development in the Arab World; Which Way Forward, British Medica Journal, http://www.bmj.com/cgi/content/full/326/7399/1141/DC1, retrieved July 2008* [cited.
283. *Middle East Times, Mideast Fertility Rates Plunge, Published: January 25, 2008, Middle East Times, Mymetimes.com.*
284. UNDP-POGAR. *Programme on Governance in the Arab Region Gender and Citizenship Initiative, http://gender.pogar.org/, retrieved July 2008.* [cited.
285. Palestinian Central Bureau of Statistics. *Labour Force Survey, April-June 2005. http://www.pcbs.org/press_r/labour_q205e.pdf, retrieved july 2008.* [cited.
286. Rashad, H., et. Al, . *Progress in the Arab World 2004, http://www.iknowpolitics.org/en/node/1110, retrieved July 2008* [cited.
287. World Health Organization. *Regional Health Systems Observatory / Regional Office for the Eastern Mediterranean; Health Systems Profile Jordan; http://gis.emro.who.int/HealthSystemObservatory/PDF/Jordan/Health%20status%20and%20demographics.pdf.* 2006 [cited.
288. World Health Organization. *Cooperation Strategy at a Glance, August 2006, http://www.who.int/countryfocus/resources/ccsbrief_west_bank_and_gaza_en.pdf, retrieved July 2008* [cited.

289. *http://www.drabruzzi.com/hills_criteria_of_causation.htm*. [cited.

APPENDICES

Appendix 1
Terms Used in the Literature Review Search Strategy

Coronary Disease/Epidemiology*

- Parity*
- Pregnancy
- Body Height
- Body Mass Index
- Body Weight
- Case-Control Studies
- Coronary Disease/ethnology*
- Coronary Disease/aetiology*
- Diabetes Complications
- Educational Status
- Female
- Humans
- Hypertension/complications
- Logistic Models
- Maternal Age
- Middle Aged
- Obesity/complications
- Odds Ratio
- Parity
- Prevalence
- Questionnaires
- Research Support, U.S. Gov't, P.H.S.
- Risk Factors
- Smoking/adverse effects
- United States/epidemiology
- Women's Health*
- Adult
- Coronary Disease/psychology*
- Family Characteristics
- Female
- Humans
- Infant, Newborn
- Life Change Events
- Life Style
- Menopause/psychology
- Parity*
- Pregnancy
- Prospective Studies
- Research Support, U.S. Gov't, P.H.S.
- Social Support*
- Stress, Psychological/complications*

MeSH Terms:

- Adult
- Aged
- Coronary Disease/epidemiology*
- Coronary Disease/aetiology
- Coronary Disease/genetics
- Estrogens/blood
- Female
- Health Behaviour
- Humans
- Male
- Menopause
- Parity
- Pregnancy
- Research Support, U.S. Gov't, P.H.S.
- Risk Factors
- Sex Characteristics
- Se Factors*
- Social Support
- Middle Aged

Appendix 2

Definitions, computations and coding of exposure, outcome variables, confounders and other covariates used in the study

1. Definition of CHD

CHD was defined as self report of a doctor diagnosis of myocardial infarction, angina, heart failure, valve problem and /or a record of a diagnosis of any one of these conditions.

2. Definition of the Metabolic Syndrome:

The Metabolic Syndrome is a clustering of metabolic derangements that cause affected subjects to have an increased risk for developing diabetes, cardiovascular disease, and, according to recent epidemiologic studies, chronic kidney disease. [1]

There have been four definitions of metabolic syndrome published by different national and international committees. In an effort to bridge the differences existent in those classifications, a unified definition that recognizes the increased biologic activity of the upper visceral fatty tissue and the strong association of abdominal obesity as a leading part of metabolic syndrome has been proposed by the International Diabetes Association. [2]

The International Diabetes Federation has proposed a new definition that requires the presence of central obesity with specific ethnic cut-points:

Central obesity (defined as waist circumference ≥ 94 cm for Europid men and ≥ 80 cm for Europid women, with ethnicity specific values for other groups)

Plus any two of the following four factors:

- raised triglycerides ≥150 mg/dl (1.7 mmol/L), or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L) in males and < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
- raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mmHg, or treatment of previously diagnosed hypertension
- raised fasting plasma glucose (FPG) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes.

These values apply to Eastern Mediterranean and Middle East (Arab) populations.

3. Definition of 10 years risk for developing CHD

Estimation of CHD risk for the next 10 years for each woman was based on Framingham risk scoring equation which accounts the following risk factors: age, current smoker, diabetic, SBP, total cholesterol, HDL-C.

Two steps were used to calculate the risk score:

(1) The first step was to calculate the number of points for each risk factor and then counting the total risk factors score for each woman.
(2) The second step was to classify women into 3 categories: a. those with 10 years risk for CHD of ≥ 20% defined as high risk, b. 10-< 20% defined as moderate risk, and c. those with < 10% defined as low risk. [3]

The following algorithm was used for estimating the 10 years risk for developing CHD, expressed in Stata code:

- generate lnage=ln(exact_ag)
- recode q129 1=0 2=1 3=0, gene(currsmoke)
- gene diabetic=gluc>=126
- generate muchd=15.5305+28.441-15.938*lnage+1.8515*(lnage^2)-0.9119*log(q149_h)-0.2767*currsmoke-0.7181*ln(chol/hdl)-0.3758*diabetic
- gene sigmachd=exp(0.9145-0.2784*muchd)
- gene uchd=(ln(10)-muchd)/sigmachd
- gene r10chd=1-exp(-exp(uchd))

4. Computation of Further Variables:

Family Affluence Scale (FAS) variable computation:

We created a new variable called household crowdedness which was computed by dividing the number of people living in the household by the number of rooms excluding the kitchen and bathrooms. (Q5/Q29)

This measure of household crowdedness was recoded as (lowest through 1 = not crowded) (1.01 through 2= moderate) (2.01 through highest = crowded) and this three-point scale was called household crowded scale (crowding scale).

Another variable was created called household amenities. It was computed as the sum of all the amenities mentioned in q31 (q31-1 to q31-17).

This household amenities variable was recoded into a three-point scale, with those with 0 to 5 amenities in the household given a code of 1, those with 6 amenities given a code of 2 and those with 7 or more amenities were coded as 3. This new variable was called household amenities recoded.

A further scale, called the Family Affluence Scale (FAS), was constructed from the crowding scale combined with the count of amenities for the household. The FAS had three values defined as follows:

A. For uncrowded households (one person per room or less) and for any number of amenities, the FAS was coded 3.

B. For households of moderate crowding (more than one and up to two persons per room), the FAS was also coded 3 if the number of amenities exceeded 5, but was coded 2 if there were 5 or less amenities reported.

C. For the most crowded households, with more than two persons per room, and with more than 6 amenities, the FAS was again coded as 2, but with less amenities, the FAS was coded 1.

Stress Variable Computation:

Women were asked about a series of life events that might have occurred in the past six months of their lives such as death of a family member, separation, loss of a job, etc.. Although some life events are more stressful than others, yet these life events were divided into five categories based on the effect they might exert as in A, B,C, D and E. These five categories constituted the basis for the construction of the stress scale index as follows:

A. Human loss and trauma to study subject, if a person has experienced any one of the items listed below or all combined

1. This category includes death of a spouse, and/or
2. Divorce, and /or
3. Addition of a family member, and/or
4. Marriage of spouse, and/or
5. Major personal injury or illness
6. Major change in argument with spouse
7. In-law troubles

B. Human loss and trauma to family member, if a person has experienced any one of the items listed below or all combined

1. Death of a close family member, and /or
2. Detention of any family member
3. Injury or shot of a family member
4. Major change in living conditions

C. Property loss to subject

1. Demolition of your house

D. Work related problems, if a person has experienced any one of the items listed below or all combined

1. Spouse ending work
2. Being fired from work
3. Major changes in working conditions

E. All stress events combined

A woman is coded as positive for this all events combined, if she is positive for one or more of the categories A, B, C or D.

5._Definitions and categorization of confounders and other covariates:

5.1 Definitions of confounders:

Women's age in years. Age of women was divided into 5 categories:

- 40-44 years
- 45-49 years
- 50-54 years
- 55-59 years
- 60+ years

Years of schooling for both women and their husbands were categorized as follows:

- No formal education: 0 years of schooling
- Elementary: 1-6 years of schooling
- Secondary: 7-12 years of schooling
- Higher: 12+ years of schooling

Marital status was categorized as follows:

- Single
- Married and currently living with husband
- Divorced
- Separated
- Widowed

5.2 Definitions of Other Covariates:

➲ Occupation of women was categorized into:

- Unskilled worker
- Skilled worker
- Employee
- Private business

➲ Physical activity was assessed by three questions:

- Do women practice any kind of physical exercise (yes or no)?
- If yes what kind of physical exercise do they practice?
- How many hours per week they practice?
- The first question was only used in assessing physical activity, as few women (69) were walking with a mean of 3 hours per week.

➲ Smoking was categorized as current, ex-smoker and never smoked.

➲ Hours per week watching TV was categorized into:

- ≤ 4 hours
- 5-10 hours
- 11-20 hours
- 21+ hours

➲ Assistance in housework was categorized as yes or no.

➲ Age at first marriage was categorized as < 18 years, and 18+ years.

➲ Age at first birth was categorized as ≤ 18 years, and > 18 years.

➲ Gravidity was defined as the total number of pregnancies including lost pregnancies and stillbirths.

➲ **Age at menarche** in years was categorized as:
- ≤ 11
- 12
- 13
- 14
- 15+

➲ **History of infertility** was defined as the women have ever tried to become pregnant for one straight year or more and did not become pregnant during that time. It was categorized as yes or no.

➲ Pregnancy ended as a miscarriage or abortion was categorized as yes or no.

➲ Pregnancy ended as a stillbirth was categorized as yes or no.

➲ Ever had polycystic ovaries was categorized as yes or no.

➲ Ever uses contraceptive pill (yes or no).

➲ Periods stopped now as yes or no.

➲ Age at menopause in years was categorized as:
- ≤ 44
- 45-49
- 50-54
- 55+

➲ Family history of diabetes, hypertension and CHD was classified as yes or no according to the woman's report.

➲ Gravidity was defined as the total number of pregnancies including lost pregnancies and stillbirths.

1. Reisen Efrain MD and Alpert Martin A MD, American Journal of the Medical Sciences December 2005. **330**(6): p. 269-272.
2. International, D., Federation,. *The IDF consensus world-wide definition of the metabolic syndrome. Available on line at: www.idf.org*. 2005 [cited.
3. Wilson PWF, Castelli William, and Kannel William, *Coronary Risk Prediction in Adults (The Framingham Heart Study)*. Am J Cardiol, 1987. **59**(9): p. 91G-94G.

Appendix 3
Women's Health Questionnaire

Principal Investigator: Najwa Rizkallah

1. SERIAL NUMBER:..... ☐☐☐

2. RESPONDENT'S NAME:.....

3. RESPONDENT DATE OF BIRTH: YEAR ☐☐ MONTH ☐☐ DAY ☐☐

4. AGE IN YEARS ..... ☐☐, ☐

5. NUMBER OF PEOPLE LIVING IN THE HOUSEHOLD: ..... ☐☐

6. ARE YOU: ☐

   1. married 2. single 3. divorced
   4. separated 5. widowed 6. others, specify .....

7. ARE YOU NOW ☐

   1. Pregnant 2. Not pregnant
   3. Not sure 4. Breastfeeding for the last 12 month

If the answer is pregnant, not sure, or breastfeeding, end the interview.
If not go to the next page.

CONSENT OF PARTICIPANT

Please sign below if you are interested and willing to participate in this research. We assure you that all information given by you will be kept absolutely confidential. Please note that no names of participants will be used at any stage of the research.

Thank you.

SIGNED BY..... DATE.....

INTERVIEWER'S NAME:..... DATE OF INTERVIEW:.....

PART ONE: SOCIO-DEMOGRAPHIC CHARACTERISTICS

8. **Place of birth:** ☐

1. Jerusalem 2. West Bank 3. Gaza Strip
4. Palestine 1948 5. Arab country 6. Foreign country

9. **Name the city/village/camp that you were born in .....** ☐☐

10. **How long have you been living in the camp .....** ☐☐, ☐

MARITAL STATUS

11. **Number of marriages .....** ☐

12. **Age at first marriage .....years** ☐☐, ☐

13. **How many children altogether did you have from your first or all your marriages? .....** ☐☐

14. **How many pregnancies altogether did you go through from your first or all your marriages? .....** ☐☐

PART TWO: EDUCATION AND ECONOMIC STATUS

15. **Years of schooling.....** ☐☐

16. **Do you work?** 1. Yes 2. No *(go to Q 21)* ☐

17. **What is your occupation?** ☐

1- Unskilled worker (cleaning, work in a factory, etc)
2- Skilled worker (dresser, weaving, etc)
3- Employee
4- Retired
5- Private business
6- Others, specify .....

18. **Is your paid work at:** ☐

1. Home 2. Outside home 3. others, please specify .....

19. **Do you work at:** ☐

1. UNRWA 2. Palestinian NGO 3. Palestinian GO
4. International Organization 5. Private organization 6. Private business
7. Others, specify .....

20. **Place of work:** ☐

1. Jerusalem 2. West Bank 3. Israel
4. NA 5. Others: specify .....

21. **What were your husband's years of schooling? .....** ☐☐

22. **Does your husband work** 1. Yes 2. No, go to Q. 26 3. NA ☐

23. **What is your husband's occupation?** ☐

1. Unskilled laborer 2. Skilled laborer 3. Employee
4. Private business 5. Retired 6. NA
7. Others, specify .....

24. **Does your husband work at:** ☐

1. UNRWA 2. Palestinian NGO 3. Palestinian GO
4. International organization 5. Private organization 6. Private business
7. NA 8. Others, specify .....

25. **Place of your husband's work** ☐

1. Jerusalem 2. West Bank
3. Israel 4. Outside the country, specify .....
5. NA 6. Others (specify) .....

26. **How many people altogether are working and living in this household?** ..... ☐

27. **Do you have any sources of income other than the salaries?** 1. Yes 2. No ☐

PART THREE: HOUSEHOLD CONDITIONS

28. **Do you own your house?** 1. Yes 2. No ☐

29. **Number of rooms in the household excluding the kitchen and bathrooms** ..... ☐

30. **How much is the area of your house?** ..... m^2 ☐☐☐

31. **What household amenities do you have?**

1. Colored TV 1. Yes 2. No ☐
2. Video 1. Yes 2. No ☐
3. Fridge 1. Yes 2. No ☐
4. Dip freeze 1. Yes 2. No ☐
5. Washing machine (full automatic) 1. Yes 2. No ☐
6. Dryer 1. Yes 2. No ☐
7. Dish washer 1. Yes 2. No ☐
8. Microwave 1. Yes 2. No ☐
9. Air condition 1. Yes 2. No ☐

10. TV dish	1. Yes	2. No	☐
11. Lands, Real-estate	1. Yes	2. No	☐
12. Commercial buildings	1. Yes	2. No	☐
13. Workshop	1. Yes	2. No	☐
14. Factory/ company	1. Yes	2. No	☐
15. Truck	1. Yes	2. No	☐
16. Private car, if yes specify model	1. Yes	2. No	☐
17. Taxi, if yes specify model	1. Yes	2. No	☐

PART FOUR: QUESTIONS ABOUT REPRODUCTIVE HISTORY

32. Have you ever being pregnant, even if the pregnancy lasted for a short while? ☐

1. Yes 2. No, go to Q. 67 3. NA, go to Q. 70

33. How old were you when you first became pregnant? ..... years ☐☐,☐

34. What was the interval in months between marriage and becoming pregnant? ..... ☐☐

35. How many times did you become pregnant? ..... ☐☐

36. How old were you at the time of your first live birth? ..... years ☐☐,☐

37. How old were you at the time of your last live birth? ..... years ☐☐,☐

38. How many live births have you ever had? ..... live births ☐☐

39. Have you ever experienced a pregnancy that ended as a miscarriage or as an abortion before it was due? 1. Yes 2. No, go to Q 42 ☐

40. How many of your pregnancies ended as a miscarriage or as an abortion? ..... ☐

41. Please list the date of every abortion or miscarriage that you have ever experienced

..... ☐☐	..... ☐☐	..... ☐☐
..... ☐☐	..... ☐☐	..... ☐☐

42. Have you ever experienced a pregnancy that ended as a stillbirth? ☐

1. Yes 2. No, go to Q 45

43. How many of your pregnancies ended as stillbirth (the baby didn't cry at birth)? ..... ☐

44. Please list the date of every stillbirth you have ever experienced

..... ☐☐ ..... ☐☐

..... ☐☐ ..... ☐☐

45. Please list the sex and year of birth of your children and state whether breast fed or not and the duration of breastfeeding

No	Name	Sex 1. Male 2. Female	Date of Birth	Breastfed 1. Yes 2. No	Duration in Months	S	Date D D / M M / Y Y	BF	DBF
1.						☐	☐☐/☐☐/☐☐	☐	☐☐
2.						☐	☐☐/☐☐/☐☐	☐	☐☐
3.						☐	☐☐/☐☐/☐☐	☐	☐☐
4.						☐	☐☐/☐☐/☐☐	☐	☐☐
5.						☐	☐☐/☐☐/☐☐	☐	☐☐
6.						☐	☐☐/☐☐/☐☐	☐	☐☐
7.						☐	☐☐/☐☐/☐☐	☐	☐☐
8.						☐	☐☐/☐☐/☐☐	☐	☐☐
9.						☐	☐☐/☐☐/☐☐	☐	☐☐
10.						☐	☐☐/☐☐/☐☐	☐	☐☐
11.						☐	☐☐/☐☐/☐☐	☐	☐☐
12.						☐	☐☐/☐☐/☐☐	☐	☐☐
13.						☐	☐☐/☐☐/☐☐	☐	☐☐
14.						☐	☐☐/☐☐/☐☐	☐	☐☐
15.						☐	☐☐/☐☐/☐☐	☐	☐☐
16.						☐	☐☐/☐☐/☐☐	☐	☐☐
17.						☐	☐☐/☐☐/☐☐	☐	☐☐

46. Just to make sure that I am right: you have had in total

1. Pregnancies throughout your life ☐☐
2. Live births throughout your life ☐☐
3. MISCARRIAGES and or abortions throughout your life ☐☐
4. Stillbirths throughout your life ☐☐

47. What is the average gain in weight, in kg, during each pregnancy?

1. .....kg 1st pregnancy ☐☐
2. .....kg 2nd pregnancy ☐☐
3. .....kg 3rd pregnancy ☐☐
4. .....kg 4th pregnancy ☐☐
5. .....kg 5th pregnancy ☐☐
6. .....kg 6th pregnancy ☐☐
7. .....kg 7th pregnancy ☐☐
8. .....kg 8th pregnancy ☐☐
9. .....kg 9th pregnancy ☐☐
10. .....kg 10th pregnancy ☐☐
11. .....kg 11th pregnancy ☐☐
12. .....kg 12th pregnancy ☐☐
13. .....kg 13th pregnancy ☐☐
14. .....kg 14th pregnancy ☐☐
15. .....kg 15th pregnancy ☐☐
16. .....kg 16th pregnancy ☐☐
17. .....kg 17th pregnancy ☐☐

48. What is the birth weight of your children?

1. First ..... kg ☐,☐
2. Second ..... kg ☐,☐
3. Third ..... kg ☐,☐
4. Fourth ..... kg ☐,☐
5. Fifth ..... kg ☐,☐
6. Sixth ..... kg ☐,☐
7. Seventh ..... kg ☐,☐
8. Eighth ..... kg ☐,☐
9. Ninth ..... kg ☐,☐
10. Tenth ..... kg ☐,☐

11. Eleventh ..... kg ☐,☐

12. Twelfth ..... kg ☐,☐

13. Thirteenth ..... kg ☐,☐

14. Fourteenth ..... kg ☐,☐

15. Fifteenth ..... kg ☐,☐

16. Sixteenth ..... kg ☐,☐

17. Seventeenth ..... kg ☐,☐

49. Do you think increasing your weight improves the course of pregnancy? ☐

1. Yes 2. No 3. Do not remember

50. Did you have any food cravings during any of your pregnancies? ☐

1. Yes 2. No, go to Q 52 3. Do not remember

51. If yes, what was it?

1. Salty foods (pickles and salted fish)	1. Yes	2. No	3. do not remember	☐
2. Sweet foods	1. Yes	2. No	3. do not remember	☐
3. Fruits and/ or vegetables	1. Yes	2. No	3. do not remember	☐
4. Dairy products	1. Yes	2. No	3. do not remember	☐
5. Fish	1. Yes	2. No	3. do not remember	☐
6. Meat	1. Yes	2. No	3. do not remember	☐
7. Others, please specify.....	1. Yes	2. No	3. do not remember	☐

52. Did any of the children have any diseases or accidents at birth? ☐

1. Yes 2. No 3. Not sure

PART FIVE: BREAST FEEDING PRACTICES

53. How long do you think a mother should breastfeed her child? .....months ☐☐

54. In your opinion, breast milk is: ☐

1. More nutritional and healthier 2. The same
3. Less nutritional than bottle milk for the child 4. Don't know

55. What are/were your sources of information on breastfeeding?

1. Mother	1. Yes	2. No	☐
2. Friends	1. Yes	2. No	☐

3. TV/ magazines 1. Yes 2. No ☐
4. Books/education 1. Yes 2. No ☐
5. Doctor/nurse 1. Yes 2. No ☐
6. Experience 1. Yes 2. No ☐
7. Holy Quran 1. Yes 2. No ☐
8. mother in law 1. Yes 2. No ☐
9. Others, specify..... 1. Yes 2. No ☐

56. Following the first delivery, what were your feelings towards breastfeeding prior to initiation? ☐

1. Anxiety 2. Shyness 3. Confidence
4. Inconvenience 5. I don't know 6. Others, specify.....

57. Did you experience any problems with the initiation of breastfeeding? ☐

1. No problems 2. Pain 3. Poor flow
4. Cracked nipple 5. Inverted nipple 6. Others, specify.....

58. What effects did breastfeeding have on you? ☐

1. physically tiring 2. loss of weight 3. breast engorgement
4. gain weight 5. insufficient flow 6. embarrassment
7. others, specify.....

59. Are you aware that breastfeeding has a contraceptive effect? ☐

1. Yes 2. No, 3. Not sure

60. Are you aware that that weight gain during pregnancy is partly for breastfeeding? ☐

1. Yes 2. No 3. Not sure

61. Were there special groups of foods consumed (e.g. to increase milk flow) during lactation? ☐

1. Yes 2. No, go to Q 64 3. Not sure, go to Q 64

62. If yes, is it

1. Dairy milk 1. Yes 2. No ☐
2. Vegetables/ fruits 1. Yes 2. No ☐
3. Carbohydrates 1. Yes 2. No ☐
4. Meat group, eggs and legumes 1. Yes 2. No ☐
5. Liquids 1. Yes 2. No ☐
6. Sweets and confectionaries 1. Yes 2. No ☐
7. Others, specify..... 1. Yes 2. No ☐

63. The source of advice to consume these foods is from

1. Mother in law	1. Yes	2. No	☐
2. Mother	1. Yes	2. No	☐
3. Friends/neighbors	1. Yes	2. No	☐
4. Formal education	1. Yes	2. No	☐
5. Doctor/nurse	1. Yes	2. No	☐
6. Experience	1. Yes	2. No	☐
7. Family	1. Yes	2. No	☐
8. TV/radio/magazines	1. Yes	2. No	☐
9. Dietition	1. Yes	2. No	☐
10. Others, specify.....			☐

64. Were there special groups of foods avoided (e.g. that affect milk flow) during lactation? ☐

1. Yes 2. No, go to Q. 67 3. Not sure, go to Q. 67

65. If the answer is yes to the above question, what are/were the food groups

1. Hot chilies, Pickles, Spices, Onion, Legumes	1. Yes	2. No	☐
2. Tea, Coffee, Fizzy drinks, Fruits & Vegetables juices	1. Yes	2. No	☐
3. Water	1. Yes	2. No	☐
4. Fish	1. Yes	2. No	☐
5. Meat	1. Yes	2. No	☐
6. Others, specify.....	1. Yes	2. No	☐

66. The source of advice to avoid these special foods is from

1. Mother in law	1. Yes	2. No	☐
2. Mother	1. Yes	2. No	☐
3. Friends	1. Yes	2. No	☐
4. Formal education	1. Yes	2. No	☐
5. Doctor/nurse	1. Yes	2. No	☐
6. Experience	1. Yes	2. No	☐
7. Family	1. Yes	2. No	☐
8. TV, magazines	1. Yes	2. No	☐

9. Dietitian 1. Yes 2. No ☐

10. Others, specify..... 1. Yes 2. No ☐

History of Infertility

67. Did you have any problems getting pregnant (Have you ever tried for one straight year or more to become pregnant and during that time not become pregnant? ☐

1. Yes 2. No

If the answer is yes, please specify ..... ☐

68. Have you had any tests because of difficulty getting pregnant? 1. Yes 2. No ☐

If the answer is yes, please specify ..... ☐

69. Have you had any treatment for fertility problems? 1. Yes 2. No ☐

If the answer is yes, please specify ..... ☐

70. About how old were you when you had your first period? .....years ☐☐, ☐

71. Have your periods generally been ☐

1. Regular 2. Slightly irregular (sometimes missing a period when not pregnant
3. Not sure 4. Very irregular (often missing one or more periods when not pregnant

72. Have your periods stopped now? ☐

1. Yes 2. No, please go to Q. 75

73. About how old were you when you had your last period? ..... Years ☐☐, ☐

74. Why did your period stop? ☐

1. Natural menopause 2. Hysterectomy (womb removed at operation)
3. Ovaries removed at operation 4. Hysterectomy and ovaries removed at same operation
5. Prescribed medical treatment 6. Other, please specify .....

75. Have you ever had a cervical smear test? ☐

4. Yes 5. No, go to Q. 77 6. Not sure, go to Q. 77

76. If the answer is yes, when was that? (before how many years) ..... ☐☐, ☐

77. Have you ever had a mammogram (an X-ray of your breasts)? ☐

1. Yes 2. No, go to Q. 79 3. Not sure

78. If the answer is yes, when was that? (Before how many years) ..... ☐☐, ☐

79. Have you ever use the contraceptive pill? ☐

1. Yes, but not taking it now 2. Yes, taking it now 3. No, please go to Q.81

80. For how long have you been taking the pill? ..... ☐☐, ☐

81. **Have you ever used Hormone replacement Therapy (HRT)?** ☐

1. Yes, but not taking it now 2. Yes, taking it now 3. No, please go to Q.84

82. **What type of HRT did you use?**

1. Estrogen 1. Yes 2. No ☐
2. Progesterone 1. Yes 2. No ☐
3. Both 1. Yes 2. No ☐

83. **Roughly for what total length of time have you used HRT?** ..... years ☐☐,☐

84. **Have you ever had polycystic ovaries?** ☐

1. Yes 2. No 3. Not sure

PART SEVEN: QUESTIONS ABOUT YOUR HEALTH

85. **How would you describe your general health?** ☐

1. Very good 2. Good 3. Average
4. Poor 5. Very poor

86. **Have you been told by a doctor or a nurse that you have any of the following:**

86/1 HIGH BLOOD PRESSURE 1. Yes 2. No ☐

A. Were you pregnant when you were told that you had high blood pressure? 1. Yes 2. No ☐

B. Have you ever had high BP apart from when you were pregnant? 1. Yes 2. No ☐

If No, go to Q. 86/2

C. Apart from when you were pregnant, approximately how old were you when a doctor told you that you had high BP? Age. .....years ☐☐,☐

D. Are you receiving treatment for high BP? 1. Yes 2. No ☐

If No, go to Q. 86/2

E. If the answer is yes to Q. D, was the treatment

1. Diet 1. Yes 2. No ☐
2. Tablets 1. Yes 2. No ☐
3. If the answer is yes, please specify the name of the tablets ..... ☐

86/2 DIABETES 1. Yes 2. No ☐

A. Were you pregnant when you were told that you had diabetes? 1. Yes 2. No ☐

B. Have you ever had diabetes apart from when you were pregnant? 1. Yes 2. No ☐

go to Q. 86/3

C. Apart from when you were pregnant, approximately how old were you when a doctor told you that you had diabetes? Age. .....years ☐☐, ☐

D. Are you receiving treatment for diabetes? 1. Yes 2. No ☐

No, go to Q. 86/3

E. If the answer is yes to Q. D, was the treatment

1. Diet 1. Yes 2. No ☐
2. Insulin 1. Yes 2. No ☐
3. Tablets 1. Yes 2. No ☐
4. If the answer is yes, please specify the name of the tablets ..... ☐

86/3 HEART CONDITION 1. Yes 2. No ☐

No, go to Q. 86/4

A. How old were you? Age. .....years ☐☐, ☐

B. What was the condition called?

1. Heart attack/ myocardial infarction 1. Yes 2. No ☐
2. Angina 1. Yes 2. No ☐
3. Valve problem 1. Yes 2. No ☐
4. Heart failure 1. Yes 2. No ☐
5. Other, specify ..... ☐

86/4 STROKE/ Transient Ischaemic Attack 1. Yes 2. No, go to Q 86/5 ☐

A. How old were you? Age. .....years ☐☐, ☐

86/5 CANCER 1. Yes 2. No, go to Q. 86/6 ☐

A. How old were you? Age .....years ☐☐, ☐

B. Which part of your body was the cancer? ..... ☐

86/6 HAVE YOU ANY OTHER CHRONIC DISEASE? 1. Yes 2. No, go to Q 87 ☐

1/a. If the answer is yes, please specify the condition ..... ☐

1/b. Age at diagnosis ..... ☐☐, ☐

2/a. If the answer is yes, please specify the condition ..... ☐

2/b. Age at diagnosis ..... ☐☐, ☐

87. Are you taking any other prescribed medicine now? 1. Yes 2. No, go to Q. 89 ☐

88. Please list the medicines you are taking and you have not mentioned them before and the reason for taking them

1. Name of medicine ..... ☐

   Reason ..... ☐

2. Name of medicine ..... ☐

   Reason ..... ☐

3. Name of medicine ..... ☐

   Reason ..... ☐

4. Name of medicine ..... ☐

   Reason ..... ☐

89. Have you ever had your cholesterol level measured? ☐

1. Yes 2. No, go to Q 91 3. Don't remember

90. What was your cholesterol level; ☐

1. Low 2. Normal 3. High 4. Don't know

please give the number if you know ..... ☐☐☐

91. Have you ever had your Triglyceride level measured? ☐

1. Yes 2. No, go to Q 93 3. Don't remember

92. What was your Triglyceride level; ☐

1. Low 2. Normal 3. High 4. Don't know

please give the number if you know ..... ☐☐☐

93. Did you have your blood pressure measured? ☐

1. Yes 2. No, go to Q 97 3. Don't remember

94. When was the last time you have had your blood pressure measured? ..... ☐☐, ☐

95. Was your blood pressure measure ☐

1. Low 2. Normal 3. High 4. Don't know

96. Do you remember the reading of your blood pressure?

1. Systolic ..... ☐☐☐

2. Diastolic ..... ☐☐☐

SECTION EIGHT: FAMILY HISTORY

97. Has anyone in your family ever had high blood pressure (hypertension)?

1 Yes 2. No, go to Q. 99 ☐

98. If the answer is yes, was he/ she your:

1. Father 1. Yes 2. No ☐ 2. Mother 1. Yes 2. No ☐

3. Brother 1. Yes 2. No ☐ 4. Sister 1. Yes 2. No ☐

5. Children 1. Yes 2. No ☐ 6. Other, specify ..... ☐

99. Has anyone in your family ever had diabetes? 1. Yes 2. No, go to 101 ☐

100. If the answer is yes, was he/ she your:

1. Father 1. Yes 2. No ☐ 2. Mother 1. Yes 2. No ☐

3. Brother 1. Yes 2. No ☐ 4. Sister 1. Yes 2. No ☐

5. Children 1. Yes 2. No ☐ 6. Other, specify ..... ☐

101. Has anyone in your family ever had hyperlipedemia? 1. Yes 2. No, go to 103 ☐

102. If the answer is yes, was he/ she your:

1. Father 1. Yes 2. No ☐ 2. Mother 1. Yes 2. No ☐

3. Brother 1. Yes 2. No ☐ 4. Sister 1. Yes 2. No ☐

5. Children 1. Yes 2. No ☐ 6. Other, specify ..... ☐

103. Has any in your family ever had heart disease? 1. Yes 2. No, go to 105 ☐

104. If the answer is yes, was he/ she your:

1. Father 1. Yes 2. No ☐ 2. Mother 1. Yes 2. No ☐

What was it? ..... ☐ What was it? ..... ☐

3. Brother 1. Yes 2. No ☐ 4. Sister 1. Yes 2. No ☐

What was it? ..... ☐ What was it? ..... ☐

5. Children 1. Yes 2. No ☐ 6. Other, specify ..... ☐

What was it? ..... What was it? ..... ☐

☐ What was it? .....

105. Was there a blood relationship (consanguinity) between your father and your mother?

1 Yes 2. No, go to Q. 107 ☐

106. What was the relationship? ☐

1. First cousin 2. Second cousin 3. Other relationship

107. Describe your father's weight while you were growing up (12-15 years) ☐

1. Very overweight 2. Slightly overweight 3. About average
4. Slightly underweight 5. Very underweight 6. Don't remember

108. Describe your mother's weight while you were growing up (12- 15 years) ☐

1. Very overweight 2. Slightly overweight 3. About average
4. Slightly underweight 5. Very underweight 6. Don't remember

109. Describe your husband's weight ☐

1. Very overweight 2. Slightly overweight 3. About average
4. Slightly underweight 5. Very underweight 6. No applicable

110. Can you remember how much did you weigh when you were 18 years old? ..... kg ☐☐ , ☐

111. When you were about 18 years old would you say you were? ☐

1. Very overweight 2. Slightly overweight 3. About average
4. Slightly underweight 5. Very underweight 6. No applicable

112. Do you think you are ☐

1. Underweight 2. Normal weight
3. Overweight 4. Obese
5. Very obese

113. What weight do you think is appropriate for you? .....kg ☐☐ , ☐

114. What does your husband think of your weight? ☐

1. Very underweight 2. About average 3. overweight
4. Obese 5. Very obese 6. Doesn't comment
7. NA

115. Have you gained weight after marriage? ☐

1. Yes 2. No, go to Q. 117 3. Don't remember

116. If yes, how much weight in kg did you gain after marriage? ..... kg ☐☐ , ☐

117. In your opinion, what is the reason behind putting on weight?

1. Marriage 1. Yes 2. No ☐

2. Pregnancy 1. Yes 2. No ☐

3. Overeating 1. Yes 2. No ☐

4. Not enough exercise 1. Yes 2. No ☐

5. Other, specify..... ☐

118. a. What is the average weight you usually gain during pregnancy? ..... Kg ☐☐,☐

b. What is the average birth weight of your children? ..... Kg ☐,☐

119. After delivery, were you able to return to your original weight before pregnancy? ☐

1. Yes 2. No, go to Q. 121 3. Not always 4. NA

120. If yes, what contributed to your return back to your original weight?

1. Exercise 1. Yes 2. No ☐

2. Going on reducing diet 1. Yes 2. No ☐

3. Returned naturally 1. Yes 2. No ☐

4. Other, specify: ..... ☐

SECTION NINE: PHYSICAL ACTIVITY

121. Do you practice any kind of physical exercise? 1. Yes 2. No, go to Q 124 ☐

122. If yes, what type of exercise do you do: ..... ☐

123. If you are practicing any kind of physical activity, on average how many hours per week do you practice physical exercise, to improve your physical fitness and health?

..... hours ☐☐,☐

124. Do you have any physical disability which hinders you from practicing exercise?

1. Yes 2. No ☐

125. Do you usually watch TV? 1. Yes 2. No, go to Q 127 ☐

126. For how many hours per week do you watch TV? ..... ☐☐,☐

127. 126. Do you have someone to assist you with the housework? 1. Yes 2. No ☐

128. How many hours per day on average do you spend doing the housework

.....Hours ☐☐,☐

SECTION TEN: BEHAVIOURAL RISK FACTORS

129. How best do you describe your smoking habits? ☐

1. Never smoked, go to Q. 130 2. Current smoker
3. Ex- smoker

2. Current smoker ☐

1. Light= < 10 cig/day 2. Moderate= 10-20 cig/day 3. Heavy= > 20 cig/day

3. Ex-smoker 1. Smoked 1-20 cig/day 2. Smoked > 20 cig/day ☐

130. Are you a passive smoker? 1. Yes 2. No, go to Q. 131 ☐

a. Does your husband or children living with you smoke at home? ☐

1. Yes 2. No, go to Q.131

b. On average, how many hours per day are you exposed to tobacco smoke of other people such as husband, children, etc? .....Hours/day ☐☐,☐

131. A. Do you smoke nargeleh? 1. Yes 2. No, go to Q 134 ☐

132. How many times a day do you smoke nargeleh? ☐☐

133. For how long have you been smoking cigarettes or tobacco? ..... ☐☐

SECTION ELEVEN: STRESS

134. In the past six months have you experienced?

1.	Death of a spouse	1. Yes	2. No ☐
2.	Divorce	1. Yes	2. No ☐
3.	Death of a close family member	1. Yes	2. No ☐
4.	Major change in argument with spouse	1. Yes	2. No ☐
5.	Addition of a new family member	1. Yes	2. No ☐
6.	In-law troubles	1. Yes	2. No ☐
7.	Marriage of your husband	1. Yes	2. No ☐
8.	Spouse ending work	1. Yes	2. No ☐
9.	Detention of any family member	1. Yes	2. No ☐
10.	Major personal injury or illness	1. Yes	2. No ☐

11. Major change in living conditions 1. Yes 2. No ☐
12. demolition of your house 1. Yes 2. No ☐
13. Being fired from work 1. Yes 2. No ☐
14. Major change in working conditions 1. Yes 2. No ☐
15. Injury or shot of a family member 1. Yes 2. No ☐
16. Others, specify ..... ☐

SECTION TWELVE: DIET

135. Women will be divided into 5 categories according to their consumption of particular food items:

1. On most days
2. 2 or 3 times per week
3. Once a week
4. Once every two weeks or three weeks or once in a month
5. Not at all

No	Food items	Daily	Two or three days in a week	Once a week	Less than once a week	Not at all	
1	**Dairy Products**						
	Milk						☐
	Cheese						☐
	Laban (yogurt)						☐
	Labaneh						☐
2	**Animal Proteins**						
	Eggs						☐
	Lamb meat						☐
	Beef						☐
	Fish						☐
	Chicken						☐
	Turkey						☐
3	**Plant Proteins**						
	Lentils						☐
	Peas						☐

No	Food items	Daily	Two or three days in a week	Once a week	Less than once a week	Not at all	
	Dried beans						☐
	Homous						☐
4	**Cereal**						
	Bread						☐
	Rice						☐
	Spaghetti						☐
	Burghul						☐
	Potatoes						☐
5	**Fruits**						
	Fresh fruits						☐
	Fruit juices						☐
	Canned/dried fruits						☐
6	**Vegetables**						
	Fresh vegetables						☐
	Green leafy vegetables						☐
7	**Sweets and confectionary, honey and jam**						☐
8	**Oil, butter and ghee**						☐
9	**Nuts**						☐
10	**Soft drinks**						☐
11	**Coffee or tea**						☐

136. How many teaspoons of sugar do you usually add to?

1- a cup of tea	No of teaspoons……..	☐☐
2- a cup of coffee	No of teaspoons…….	☐☐
3- a cup of milk	No of teaspoons…….	☐☐

137. In total, how many cups of the following do you drink per day?

1- Tea ☐☐

2- Coffee ☐☐

3- Milk ☐☐

138. Which of the following kinds of oil do you use at home?

1. Corn oil 1. Yes 2. No ☐
2. Sunflower oil 1. Yes 2. No ☐
3. Soya oil 1. Yes 2. No ☐
4. Olive oil 1. Yes 2. No ☐
5. Butter 1. Yes 2. No ☐
6. Pure animal fat (Samn baladi) 1. Yes 2. No ☐
7. Ghee from plant origin (Samn Nabati) 1. Yes 2. No ☐

139. What do you do with the visible fat on your meat? ☐

1. Eat most of it 2. Eat some of it 3. Eat as little as possible 4. Don't eat it

140. What kind of fat do you usually use for cooking and baking?

1. Olive oil 1. Yes 2. No ☐
2. Corn oil 1. Yes 2. No ☐
3. Samn Nabati 1. Yes 2. No ☐
4. lard (Samn Baladi) 1. Yes 2. No ☐
5. Others, specify ..... ☐

141. What kind of fat do you usually use for frying?

1. Olive oil 1. Yes 2. No ☐
2. Corn oil 1. Yes 2. No ☐
3. Samn Nabati 1. Yes 2. No ☐
4. lard (Samn Baladi) 1. Yes 2. No ☐
5. others, specify ..... ☐

142. How often do you eat red meat in a week? ..... ☐☐, ☐

143. Do you regularly use? ☐

1. Full cream milk 2. Half cream milk 3. Skimmed milk
4. NA 5. others, specify .....

144. How often do you eat fruits and vegetables in a week? ..... ☐☐,☐

145. How often do you eat sweets and confectionaries in a week? ..... ☐☐,☐

146. Are you currently on a special diet? 1. Yes 2. No. go to Q 149 ☐

147. Which of the following best describe the diet you are on?

1. Slimming diet	1. Yes	2. No	☐
3. Diabetic diet	1. Yes	2. No	☐
3. Cholesterol lowering diet	1. Yes	2. No	☐
4. Low salt diet	1. Yes	2. No	☐
5. High fiber diet	1. Yes	2. No	☐
6. Vegetarian diet	1. Yes	2. No	☐
7. Others specify	1. Yes	2. No	☐

148. How many years are you on it? .....Years ☐☐,☐

149. BLOOD PRESSURE MEASUREMENTS:

	SYSTOLIC	DIASTOLIC
READING 1.	..... ☐☐☐	..... ☐☐☐
READING 2.	..... ☐☐☐	..... ☐☐☐

150. Pulse: .....

READING 1. ..... ☐☐

READING 2. ..... ☐☐

SECTION TWELVE: ANTHROPOMETRIC DATA SHEET

151. HEIGHT AND WEIGHT MEASUREMENTS

a. Standing Height without shoes Reading .....cm ☐☐☐,☐

b. Weight without shoes Reading .....kg ☐☐☐,☐

152. GIRTH MEASURES:

a. Waist	Reading.....cm	☐☐☐,☐
b. Thigh	Reading.....cm	☐☐☐,☐
c. Hip	Reading.....cm	☐☐☐,☐

BLOOD WITHDRAWAL

We will be taking a blood sample now in order to test for cholesterol, trigycerides, and blood sugar levels.

- When did you last have anything other than water to eat or drink? ..... : ..... AM/PM

- If less than 10 hours from clinic appointment, the interviewer should reschedule for blood withdrawal.
- Not done .....
- Reason .....

153. LABORATORY RESULTS OF BLOOD

No	Type of Test	Result
1.	Fasting blood sugar	☐☐☐
2.	Insulin	☐☐
3.	Total Cholesterol	☐☐☐
4.	HDL-C	☐☐
5.	LDL-C	☐☐☐
6.	Triglycerides	☐☐☐

Appendix 4
Blood Pressure Measurements and Procedures

Women were asked to roll up the sleeve of the blouse so that the upper right arm will be bare for the sphygmomanometer cuff. Each woman sat at the end of the desk with the right arm allowed to rest, palm up, and the elbow on the desk so that the anticubital fossa will level with the heart. The research nurse who was trained in hypertension detection, sat facing the sphygmomanometer, which was positioned so that the mercury column will not be visible to the participant. Two cuff sizes were available: adult and large adult. The adult cuff was wrapped around the arm and if the index line fell within the range lines it was appropriately sized, if not the larger sized cuff was used. The brachial pulse was located by palpating the artery just medial to the biceps tendon and the cuff placed so that the centre of the inflation bag as marked on the cuff laid over the artery. The cuff was connected to the sphygmomanometer, and the systolic pressure was ascertained by palpation. The bronchial artery again localized and the diaphragm of the stethoscope placed on the point of maximal impulse immediately below the cuff. Systolic and diastolic blood pressures were ascertained by auscultation of the first and fifth Korotkoff sounds respectively. All readings were taken at the top of mercury meniscus (to the nearest 2 mmHg). The measurement was repeated and the second systolic and diastolic values were recorded. The average systolic and diastolic blood pressures were subsequently calculated. The women were informed about the results and in case of a problem, women were referred to UNRWA general practitioner for further medical advice.

Appendix 5
Informed Consent Form

Translated from Arabic

Good morning! My name is ..... and my colleague's name is ..... We are performing a study on women's health. The study is looking at the long-term effect of reproduction on women's health. Here is a letter of approval for conducting the study in the Amaari and Kalandia refugee camps from UNRWA health department. If you remember that we have discussed the objectives of the study as well as the benefits and risks and the overall importance of this study before when we visited you the first time with the community leader. Would you like to participate? Of course it is up to you to decide. Everything you will tell us will be confidential, and the results of the blood tests will be confidential too. You will not be given any reward for responding to the questions that we will ask you; also no reward will be offered for performing the blood tests. Please note that there is a possibility of mild discomfort and hematoma at venipuncture. It is just a possibility but you should be aware of it. If you accept to participate, you will be given a set of written and verbal instructions about the study measurements including preparation for blood tests. An appointment will be set for my colleague and me to visit you at home again to administer the questionnaire. If the physician determines you have a condition that needs further treatment, you will be referred accordingly. If you accept to participate, we need your written consent. Please remember that all answers and laboratory investigation will be private and confidential. Thank you for being patient and thank you for accepting to participate in the study.

Appendix 6
Informed Consent Form from UNRWA
Translated from Arabic

Hello! We are happy to inform you that our colleague Ms. Rizkallah will be performing a study on women's health. She will be looking at the long-term effect of reproduction on women's health at the Amaari and Kalandia Refugee Camps. This study is very important to UNRWA and to the health of Palestinian women. As for the first time someone will explore the relationship between reproduction and coronary heart disease risk factors among women in Palestine. The study will provide data on the prevalence of CHD risk factors, it will help to understand their impact on women's lives, and will clarify the relationship between women child-bearing patterns and CHD risk factors. The study will provide basic data to support UNRWA in evidence-based decision making and allocation of health care resources, to contribute to health promotion and primary prevention of CHD among Palestinian refugee women, and to increase general awareness of the burden placed by chronic diseases, and to provide one more health rationale for reducing high fertility.

This research would also help to prioritize what is most important for women's health within limited resources available, (not just another argument for family planning, but what interventions could be most effective in the prevention and treatment of these women).

Understanding the unique aspects of risk for Palestinian women will increase the awareness of women and medical caregivers and will pave the way for primary prevention efforts.

So will you like to participate in the study? If you do, you will be given a set of written and verbal instructions about all study measurements including preparation for blood tests. An appointment will be set for a trained interviewer and the principal investigator, to visit you at home and administer the questionnaire, and as UNRWA Health Department, we will be involved in the different stages of the research.

If you happen to be a case, you will be referred to UNRWA clinic for further investigation.

Remember that all study procedures including the laboratory tests to be performed, the administration of the questionnaire, will be confidential. If you accept to participate, we need your written consent. Please remember that all answers and laboratory investigation will be private and confidential.

Thank you for your participation and cooperation.

Health Department
UNRWA West Bank field of operations

Appendix 7
INFORMED CONSENT FORM Signed by Participants

This is to certify that I, _____, hereby agree to participate as a volunteer in the study under the supervision of the principal investigator Ms. Rizkallah. This study has been defined and fully explained to me by UNRWA medical officer and the principal investigator.

Health department at UNRWA	Study participant
Signature	Signature